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ON CHANGES IN DILATATION AND SIGNS OF ASPIRATION IN FETAL AND NEONATAL LUNGS

AN EXPERIMENTAL AND HISTOLOGICAL STUDY

BY

E. K. AHVENAINEN

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HELSINKI 1948

FROM THE CHILDREN'S CLINIC OF THE UNIVERSITY, HELSINKI. CHIEF: PROF. A. YLPPÖ AND FROM THE DEPARTMENT OF PATHO — ANATOMY OF THE UNIVERSITY, HELSINKI. CHIEF: PROF. A. SAXÉN

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ACADEMIC DISSERTATION

TO BE PRESENTED WITH THE ASSENT OF THE MEDICAL FACULTY OF THE UNIVERSITY OF HELSINKI FOR PUBLIC EXAMINATION IN AUDITORIUM XII ON MAY 29TH, 1948, AT 12 O'CLOCK NOON

HELSINKI 1948

Also published as a supplement to Acta Paediatrica.

Helsinki 1948. Sanoma Oy.

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INTRODUCTION

At the suggestion of Professor A. YLPPÖ I began in 1941 my researches into the questions connected with the aeration of the lungs of newborn infants, using patho-anatomic methods of research. My work was interrupted by the war in June of that year, and I was able to resume it at the beginning of 1945. — It gives me great pleasure to express my deep gratitude to Professor A. YLPPÖ, for his valuable advice in the course of my work and his unfailing interest and encouragement.

My work has been mainly carried out at the Patho-Anatomic Institute of the University, Helsinki. I wish to express my most sincere thanks to the Head of the Institute, Professor A. SAXÉN, for his guidance, both in the choosing of methods and the estimation of the results. — My thanks are due to Professor U. UOTILA, for the valuable suggestions I have received from him.

I also wish to thank the assistant Doctors of the Institute for their valuable support — especially Dr. V. RITAMA, with whom I have had the repeated pleasure to discuss my work and to receive from him invaluable advice.

I am also indebted to Dr. C.-E. RÄIHÄ, especially for his help in questions of physiology.

The material has been partly collected at the I and II Women's Clinic of the University, Helsinki and at the Midwives' College. I whis to express my deep gratitude to the Chiefs of these institutions, Professor M. RAURAMO, Professor A. TURUNEN, and Professor A. APAJALAHTI.

I wish to thank the laboratory nurses who have prepared part of my sections, for their work executed with great care. My special thanks are due to Mrs. M. HELLMAN, who has carried out the main part of the fat stainings.

I am further indebted to all those of my colleagues at the Children's Clinic and the Patho-Anatomic Institute, who have in many ways assisted me in my work — and especially to Mr. S. HEINO, for his tender care of the test animals.

I wish to express my best thanks to Mrs. E. HARDEN for her English translation of my Finnish original.

My researches have been aided by a scholarshipp from the Finnish Culture Fund (Suomen Kulttuurirahasto) and from the Research Fund for Children's Diseases (Lastentautien Tutkimusrahasto).

Helsinki December 1947

E. K. Ahvenainen

I Survey of Literature

1. Atelectasis

JÖRG (1835) was the first to describe the persisting fetal condition of the lungs in infants, he called it Atelectasis or Pneumonatelectasis and determined it as »in unvollkommener Ausdehnung oder Erweiterung der Lungen durch Luft». JÖRG separated the atelectasis from other pulmonary changes in the newborn and proposed a new name to discriminate between it and such pathologic states as »»*hepatisatio, induratio, concretio* etc.» According to JÖRG,atelectasis was always a persistence of the intra-uterine state of the lungs and a secondary atelectasis was unknown to him. According to our conception of to-day, he attributed to atelectasis a much too great and independent a part. Before JÖRG, as early as in the 17th century — a difference was observed between the lungs of the fetus and of an infant who had breathed (HARVEY) and the importance of this difference in regard to medical jurisprudence, where cases of infanticide were concerned, was also realised, by examining the capacity of the lung to float. (SCHREYER, BARTHOLINUS). Several publications described lungs of children who had breathed, found to be entirely or partly airless (ZELLER, SCHENCK, BILLARD, PIEPER). It is possible that some of them had atelectasis, but it was not clearly differentiated from other conditions and there was no plain conception as to its etiology. In any case, JÖRG has the credit of having inventend the name Atelectasis and disconnected this state from other pulmonary diseases of the newborn. The discovery of secondary atelectasis is attributed to the Frenchman LEGENDRE. He examined older children (2 to 5 years) and found that their lungs were similar to fetal lungs. Contrary to JÖRG's point of view, he was of the opinion that it was not a

question of lungs having remained in the fetal state, but of lungs having reverted to it. He applied to this the name of *»état fétal de poumon»*. He considered that JÖRG was wrong in his theory. In the first half of the 19th century TRAUBE had drawn attention to atelectasis in adults and made experimental researches on atelectasis. RUFZ had also made observations on a similar condition, without however differentiating it from the others. WEBER (1851) found that atelectasis should not as a rule be considered as a cause of neonatal death. The cause of atelectasis should always be sought and it is often to be found in the central nervous system.

Further, several observations show that at a post mortem examination also the lungs of such an infant can be airless who is known to have breathed and even cried after the delivery (NIKITIN, ORFILA, TAYLOR, WINTER, WOLF etc.). In order to explain these observations, the theory was propounded earlier that the lungs had never become expanded, and that even the crying had originated from air which had entered the bronchi. (v. SIEBOLD, MASCHKA, BREFELD, FALK, PINCUS, HECKER, ERMAN), or that the lungs had become atelectatic in a secondary manner, in such a way that less air was drawn into the lungs at inspiration, than expelled from them at expiration (THOMAS, SCHRÖDER). — In his experiments on animals, LICHTHEIM (1879) was able to find such a region becoming atelectatic, where the bronchus conducting to it was occluded, he also noted that different kinds of gases escaped from this region with different rapidity, oxygen and carbon dioxide being quicker and nitrogen slower to disappear than air. On the basis of these experiments LICHTHEIM arrived at the conclusion that secondary atelectasis appears in the lungs through the resorption of air into the blood. By filling the lungs of newborn rabbits with oxygen, UNGAR produced in them a secondary macroscopic airless condition. By poisoning the animals with curare, he obtained in his experiments a nearly complete airlessness of the lungs, as the young died slowly and respiration was arrested before the heart function stopped. HELLER (1914), plugging the bronchus of dogs, produced an atelectasis that began in the central parts of the lungs. The atelectasis was the slower to disappear after the removal of the obstruction the longer the obstruction was allowed to stay. VAN ALLEN and ADAMS found, while experimenting with dogs that atelectasis was

born only when the breathing was strained, and that valvular obstruction produced it more rapidly than did total obstruction. They found, as HELLER had done, that atelectasis was born centrifugally. According to their conclusions, »pent up bronchial air is probably lost from the lung by the blood stream absorption». It is worthy of remark that GAIRDNER (1850) believed atelectasis to appear through the valvular obstructive effect of mucus in the bronchi. According to HANSON and SJÖSTRAND, the genesis of atelectasis is a complicated process, which they felt they could not explain on the basis of animal experiments.

In the above experiments, with the exception of UNGAR's investigations, atelectasis was caused by plugging the bronchus or by producing a pneumothorax, and therefore their application to the atelectasis found in the newborn is not quite plain straight away, as there may be other contributory factors than obstruction of the bronchi.

When the opinion became generally adopted that atelectasis could also be a secondary state in the lungs, the question arose whether the atelectatic regions often or nearly regularly (THAYSEN) found in the lungs of the newborn, were of a congenital origin, or appeared in a secondary manner. Another question connected with this is how soon congenital atelectasis disappears. JÖRG noticed already that lungs could be fully expanded »bald nach der Geburt» and there are several later observations on how the lungs of the newborn can be fully expanded, even if the infant had lived but shortly (STRASSMANN, G., YLPPÖ, FRITSCH). According to some investigators, on the other hand, there are congenital atelectatic regions in the lungs of infants several weeks old (TRAISMAN, ROSE). UNGAR has maintained that when estimating different results, it must be taken into consideration that a different idea is obtained when examining the air-containing condition of the lungs of infants who had died in hospital, than in medico-legal cases of infanticide, as the former were often weak, whereas the latter might be strong infants who had died suddenly. Attemps were also made to establish by means of post-mortem material whether atelectasis was to be regarded as congenital or arisen in a secondary way. Mention has already been made of the divergent opinions of the 19th century. It can be said that later workers are divided into two opposite

groups. The one considers that lungs fully expand soon after delivery and the atelectasis is mainly or entirely secondary (Ungar, Ylppö, Loeschke, Klein, Seydel, Schmorl, Eckervogt, Kjerulf, Kathe, etc.), while according to the other, the expansion of the lungs is gradual process and atelectasis a persistence of the intrauterine condition. (Peiser, Canelli, Coryllos, Henderson, Rose, Potter, Siegel).

Addison and How have examined the expansion of the lungs by means of animal experiments on dogs. They measured in a microscopic section the comparative amount of spaces in proportion to the lung tissue and arrived at the result that the expansion was gradual. In a section taken from the lungs of a newborn young after respiration had occurred, the expanded spaces were of a different size in different regions of the lungs. Older young had comparatively more expanded space than the younger animals. The same results were obtained by Snyder and Rosenfeld in their experiments with rabbits. For a differentiation between primary and secondary atelectasis, endeavours were made to employ histologic methods of research. Before making a report on these researches, it seems advisable to give a short exposition of the fetal development of the lung, as it is essentially connected with the changes occurring at the moment of birth. — I omit the older researches, even extensive ones (e.g. Flint) and confine myself to presenting the viewpoints of only a couple of investigators. It seems that Bender must be regarded as most important, his researches gave a consistent picture of the fetal development of the lungs, and his opinion seems to be practically universally and unanimously adopted (e.g. Heiss). Bender examined the fetal development of human lungs, beginning with an embryo of 9 weeks. At this stage the fetal lungs show an epithelial tubular system in a loose mesenchymal tissue. The ends of this tubular system, »Endknospen», are dilated and far from each other, separated by the said mesenchymal tissue. In these a nearly regular dichotomic division can be perceived. Bender called the »end-buds» pneumonomeres. The pneumonomeres have a large cavity, with a high prismatic epithelium. In the preterminal passage the epithelium is flatter than in the pneumonomeres, and the central parts have again a high epithelium.

The growth takes place solely under the influence of the dichotomic division in the pneumonomeres, but if disturbances occur in the evolution, this can lead to »Mehrlingsbildungen». Also in the usual dichotomic division one »Tochterknospe» is often larger than the other, i.e. asymmetric forms appear. The growth continues on the same principle, even if the number of asymmetric formations and »Mehrlingsbildungen» varies at different developmental stages. In the process of the development the capillaries increase and the mesenchyme decrease. An embryo 6 to 7 months old has a quite flat epithelium in the »Gangabschnitt», but a »helles kubischzylindrisches Epithel» in the pneumonomeres. In his researches on the late fetal stage Bender recurred to observations on the development of the lungs in the fetus of a cat, because it was difficult to observe the human fetus in its final stages of development, and as the lung of the cat greatly resembles the human lung, even if it is of a simpler structure. He was then able to establish that the sort of development described above continued until the end of the fetal life. In Bender's opinion, the growth of the lungs after birth continues in the same way as in the intra-uterine existence. In the pneumonomeres of the newborn a high epithelium is to be found, and they are incapable of gas metabolism. The s.c. respiratory epithelium is then to be found only in the end passages («Endgänge»), where the exchange of gases takes place.

According to Broman, the premature infant breathes with his bronchioli, and the alveoli are only born passively during extra-uterine existence »als Ausdehnung der betreffenden Bronchialzweigende an denjeningen Stellen, wo diese dünn geblieben sind.»

The changes in the layer of cells covering the inside of the alveoli at the onset of breathing as well as its character in the adult have been an object of research in the second half of the 19th century. While some investigators found the inside to be covered in adults by an uniform epithelium (Chrzonszcewsky, Colberg, Elenz), others considered it dissimilar (W. Addison, Donders, Eberth, Hertz, Arnold, Weber, Virchow) and a third group came to the conclusion that there was no epithelium on the inside of the alveoli (Th. Addison, Rayney, Zenker, Bakody, Henle,

Munk). Those who had examined fetal lungs were generally of the opinion that at that stage there was epithelium in the alveoli (Weber, Colberg), which therefore was there after birth, uniform or dissimilar. The viewpoints were mainly based upon the results of researches on animals, although some examinations of human lungs were also made. (Weber, Colberg, Arnold). The reason for the great changes in the human fetus at births was considered to lie in the onset of breathing (Küttner). This change was further explained by surmising that its reason lay in the expansion of cells caused by expanding walls (Jalan de la Croix); the cells were prepared for this expansion by the formation of mucus within them towards the end of the fetal condition (Colberg). In any case, the final result of the researches of the 19th century remained that breathing is of great importance for the changes in the epithelium (Koelliker). This opinion previled up to about the 1920-ies, and the same result was arrived at also by many workers during the first two decades of the present century. (Peiser, Marx, Addison and How, Strassmann, G.), although such a viewpoint was also expressed that the changes in the epithelium are gradual after the onset of breathing (Ridella).

Ogawa (1920) has made a thorough examination of the development of the alveolar epithelium in the vertebrate and come to the conclusion that the change in the epithelium proceeds in accordance with the laws of evolution already in the fetal stage, and is not the result of the effect of breathing, although the cells become more flattened than before after the onset of respiration. The varied character assumed by the epithelium is also due to this evolution and is not the result of mechanical factors. Stewart (1923) came to the result on the basis of examinations of rats that a hydropic transformation and fatty metamorfosis take place in the epithelium, which makes it adaptable, while under the influence of the breathing movements it becomes more flattened and part of it comes off, which leaves the capillaries free. According to Stewart, the changes in the cells are probably also due to intra-uterine respiratory movements. Fauré-Fremiet (1920) believes that the changes of the alveolar epithelium are due to evolutions in the growing process and not to aerodynamic forces. Researches on fetal conditions have during these last decades led to the generally adopted opinion

that the epithelium, uniform in the early stages of development, gradually becomes varied (Clements, Barnard and Day, Cooper, Dogliotti, Siracusa etc.). This change is due to the dissimilar growth of the connective tissue and the epithelium (Seemann, Clara) but the dehiscence of the epithelium can also be due to the development of capillaries (Clements). The epithelium assumes this character in the course of the 6th to 7th fetal month and the capillaries then get in touch with the alveolor lumen, after having been so far separated from them by the uniform epithelial layer and farther from the epithelium (Clara, Palmer, Barnard and Day, Dogliotti). Also now there is a divergence of opinion as to whether the epithelium is retained after birth, or whether it disappears completely. (Clements, Norris and collaborators), in which case it would only have a canalisation function. (Barnard and Day). It is still a matter of dispute whether there is epithelium in the alveoli of the adults, and what kind of an epithelium, and whether its cells are of an epithelial or mesenchymal origin. I do not consider it necessary to go into the extensive literature dealing with this and the question of the origin of alveolar phagocytes, these being beyond the scope of my research. — The number of the cubic cells lining the fetal alveoli »end-buds» decreases toward the end of the fetal period and assertions have been made that the reciprocal relation among the number of cells of different shapes is some kind of a criterion for the viability of the child (Zeldes). Bensley and Groff found by means of researches on rats that the changes in the epithelium take place just a little before birth and soon after. On the other hand, the structure of the lungs of the human fetus has been found to be the same in the 6th to 7th month as in the newborn (Siracusa), but it has also been maintained that it is possible to distinguish different phases in the adult alveoli (the static and the dynamic phase), when the relation between the epithelium of the walls and the capillaries is subjected to changes (Costa). The opinion of Rose, that lungs are of a dual origin, with a separate appearance of alveoli and capillaries, and separate of bronchi, has not gained support. After the onset of respiration the high epithelium of the pneumonomeres disappears, according to Heiss, although he does not consider the postfetal evolution of the lungs as fully explained.

Differentiation between congenital and secondary atelectasis. — The determinations of congenital atelectasis in the textbooks and manuals are often very short, sometimes completely omitting the histologic picture. Ziegler (1890 and 1906) only mentions that if the respiration is defective, some regions remain airless, which is then a case of congenital atelectasis (»fötale Atelektase oder Apneumatosis»). Herxheimer (1910) determines atelectasis as »Zustand der Lunge, in welchem diese ganz oder in einzelnen Abschnitten luftleer ist, in welchem die Alveolen also zusammengesunken sind und die Alveolarwände einander anliegen.» Kaufmann's (1911) determination is as follows: ». . . . . die Alveolen eines Lungenabschnittes luftleer, sie haben keine polygonale Gestalt, sondern ihre Wände liegen aneinander. »Aschoff (1923) does not specify the histologic picture, but states that the lungs remain in the fetal unexpanded condition. Loeschke (1928) gives the following definition: »Als Atelektase bezeichnet man den Zustand, in dem sich die Lungen am Ende der Fötalzeit bezw. bei der Geburt vor dem ersten Eindringen von Luft befinden. Die angeborene Atelektase bedeutet also ein vollständiges Fehlen der Entfaltung der Lunge oder einzelner Teile derselben . . . .». Loeschke says however that there can be a lumen in the alveoli of the still-born, full of amniotic fluid, and therefore the »Entfaltung» of the lungs begins already to some extent before birth. Ribbert (1913) regards atelectasis as a complete airlessness of the lungs, and Hamperl's (1944) definition is equally short. Boyd (1934) presents a microscopic picture: »It resembles a secreting gland and is composed of gland-like spaces lined with cubical epithelium and separated by an abundant stroma». Beattie and Dickson (1943) as well as Bell (1944) determine atelectasis as a condition, where the lung is airless and the alveoli unexpanded. Bell says that the walls of the alveoli are »in close contact». Bergstrand determines atelectasis as a state, in which the air contents of the lung are reduced or have disappeared (»lungvävnadens lufthalt är minskad eller upphävd»), but he makes no separate mention of congenital atelectasis. The histologic difference between congenital and secondary atelectasis is not mentioned at all in the abovenamed textbooks.

As to determinations of atelectasis made by individual workers or conceptions of the histologic characteristics of atelectasis, one

only finds in literature short references to them, or such references are entirely absent. Some investigators have observed that there are alveolar lumina in the lungs of still-born infants or animals (Addison and How, Snyder and Rosenfeld, Preuss) that can even be measured and is according to measurements made by Addison and How, 20—30 % of the entire area in dogs. Others admit that there are narrow spaces in a nearly compact tissue (Marx). Barnard and Day do not say anything about the lumen, but it is very distinct in the alveoli on the microphotograph of fetal lungs presented by them. Whitehead and his collaborators came to the conclusion that the guinea-pig fetus did not have any alveolar lumen, but that it appeared only if the fetus aspirated or breathed — the lumen to be found in the alveoli of the human fetus they considered also to be due to aspiration. Even in such cases where congenital larynx atresia was present, expanded — even very much expanded — alveoli have been found. (Frankenberger, Kovacs). Artificially appearing changes have been considered the reason of the apparent spaces, which are only demonstrable in frozen but not in celloidin sections (Schönberg) — artificially produced spaces are however discernible from those due to inspiration of air (Orsos), and findings of small spaces in lungs with secondary atelectasis prove that the lung is not completely airless (Fenger). Orsos is of the opinion that the differentiation is easiest macroscopically — by examining whether there are on the surface air-containing alveoli and by pressing into them such air as might be found in the lung. Attempts have been made to achieve differential diagnosis by examining elastic fibers; it is then considered that a stronger staining or greater stretching of the fibers are characteristic for lungs that have breathed (Böhmer, Foerster).

Peiser maintains that it is possible to determine, judging from the shape of the alveolar epithelial cells whether the infant had breathed or not, as according to him a cell is flattened by respiration and cannot reassume its cubical shape, even if the air escapes from the alveoli. Farber and Wilson have made thorough examinations of the histological difference in ininitial (congenital) and resorption (secondary) atelectasis. They examined the question both experimentally and on the basis of human post mortem material

By distending the lungs of a still-born child in a Drinker respirator they were able to find that the alveolar lining cells changed from their cuboidal shape in the fetal state and became flattened, and their regular arrangement disappeared, so that when the air was lost again in consequence of secondary atelectasis, the distribution of the cells in the alveolar epithelium was uneven and the shape of the cells had lost its cubical form belonging to the fetal stage, having now become irregularly flat. They consider to have proved thereby that »The cells lining the collapsed alveoli were flattened, irregular in position and unevenly spaced along slightly tortuous alveolar walls, as contrasted with the regular even spacing of cuboidal epithelial cells lining an alveolus which has never been expanded.» In prematures they found masses of epithelial cells without alveolus formation.

The post mortem material is an unrealiable basis for estimating the capacity to become air-containing in the lungs of the newborn, if only due to the circumstance that such infants who have died within the first few hours or days have breathed but weakly. Therefore attempts have been made to find out with the help of roentgenologic examinations how soon the lungs expand after birth. Ylppö ascertained that air was to be found everywhere as early as 5 minutes after birth, and 40 minutes after it the air contents had already increased. Dunham found atelectatic regions in 4 of the 6 cases he examined. According to Wasson's researches the lungs can be completely expanded as early as 5 minutes after birth, but in some cases atelectatic regions could be found even in two weeks old infants. These investigations showed that the rapidity with which the atelectasis disappeared had much to do with the character of the delivery. The results of other authors vary greatly (Weymuller and collaborators, Solis-Cohn and Druck, Dunham and Amico, Farrell), but it seems that some atelectasis is to be found several days after birth. The roentgenologic examination is however a rather crude method in this respect, and it fails to show up small atelectatic regions (Ylppö).

Attempts have been made to estimate the expanping capacity of the lungs by measuring the volume of respiration. The older researches are unreliable owing to technical difficulties (Reckling-

HAUSEN). DOHRN came to the conclusion that the expansion of the lungs was a gradual process. The improved methods of later years have yielded more reliable results. These investigations prove that the volume of breathing increases in the first days of neonatal life (DEMING and HANNER, DEMING and WASHBURN, MURPHY and THORPE). However, the inspiration when crying on the first day of life is superior or equal to that on the tenth day (DEMING and WASHBURN) — this has already been pointed out by YLPPÖ, chiefly on the basis of clinical observations; he mentioned this in support of the rapidity of the expansion of the lungs, contrary to the results then obtained by measuring the volume of breathing.

On the Causes of Atelectasis. — The cause of congenital atelectasis was held to be the immaturity of the respiratory centre, (PEIPER, CORYLLOS, POTTER) cerebral hemorrhages (STILL, BREFELD, KJERULF, DETRÉ and collaborators, POTTER) or malformations of the brain (POTTER) — but LEVINSON and SAPHIR did not find any relation between atelectasis and cerebral hemorrhages. In addition, atelectasis has been attributed to obstructions in the bronchi due to aspiration of the amniotic fluid in the intrauterine stage or in the delivery (SNYDER and ROSENFELD, CORYLLOS, BAUER, DEKKER-JONKER etc.), to the general weakness of the baby (GERHARDT), to cohesion of the moist surfaces of the air passages (FARBER and WILSON, BAUER, CORYLLOS). Causes of the appearance of secondary atelectasis are partly the above-mentioned, but there are added to them a gradually progressing fatigue of the respiratory muscles (YLPPÖ), stasis due to a weak heart (YLPPÖ). There should also be considered obstructions of the bronchi by mucus due to inflammatory processes (BARTELS, GERHARDT). As to atelectasis of the premature in particular, part of the above-mentioned factors have perhaps an even stronger effect in their case (muscular enfeeblement appears more easily than in healthier infants — cerebral hemorrhages are more common than in fullterm babies). In addition to these factors, it must be further considered, where prematures are concerned, that the pulmonary tissue itself is immature and therefore unable to expand (FARBER und WILSON). NORRIS et col. were of the opinion that the immaturity of the lungs is not in itself a

cause of impeded breathing — the development of the lungs corresponding to the development as a whole.

Potter says that even if the factor to which atelectasis is due is not always found, the latter is not enough to cause death. It must be added in this connection that a deficient function of the lungs may sometimes have a injurious effect on the functioning of the respiratory centre (Creutzfeld and Peiper), which makes the whole process considerably more complicated.

2. Intra-Uterine Breathing and Aspiration of the Amniotic Fluid

The first animal experiments, concerning fetal respiratory movements seem to have been made by Vesalius (1542). Several scientists observed the intra-uterine breathing movements of the fetus in animal experiments made in the course of the 17th and 18th centuries (Plater, Haller, Winslow); the reason of the respiratory movements was considered to lie in an interruption of the blood circulation between fetus and mother (Whytt, Darwin). Amniotic fluid substances were found in the respiratory passages of the fetus and the newborn (Röderer). Scheel (1798) supposed that the human fetus normally in- and expirates amniotic fluid, which remains in the lungs at birth and disappears from them through evaporation and resorption. Beclard (1814) found in his experiments performed upon animals that the respiratory movements of the fetus became stronger if the circulation of the blood between it and the mother was purposely impeded. Mayer (1824) did not consider intra-uterine respiratory movements normal. When exploring the cause to which the onset of breathing was due, numerous experiments with animals were made and deliveries observed; in the early 19th century these researches formed the basis for observations on intra-uterine respiratory movement (Voltolini, Preyer, v. Franque, Kehrer, Lahs, Zweifel, v. Preuschen, Pflüger, Heinricius, Engström), the opinions diverging both with regard to the cause of the onset of respiration and the intra-uterine respiratory movements. Schwartz (1858) considered the amniotic fluid to be found in the respiratory passages as a sign of intra-uterine asphyxia to which the aspiration of the amniotic fluid was due. Schultze

(1866, 1871) was of the opinion that the fetus can become asphyxial without aspiration and on the other hand, a transient asphyxia with aspirated amniotic fluid is possible, when the infant is born in good condition, with amniotic fluid in the respiratory passages, Küstner (1877) was the first to establish pneumonia as a consequence of intra-uterine aspiration. By means of animal experiments, it was possible to demonstrate that a coloured substance injected into the amniotic sac penetrated into the lungs of the fetus, but only in case of a disturbance of the placental circulation (Geyl, Preyer).

Ahlfeld expressed his opinion in 1888 that the human fetus makes intra-uterine respiratory movements. It had already earlier been observed that there were repeated movements in the abdominal wall of a pregnant woman, and it was thought that these were sucking movements or singultus of the fetus, (Mermann, Reubold). Ahlfeld's viewpoint was based on his having observed rythmical movements in the abdominal wall of pregnant women that he could register and prove to be of the same type as the respiratory movements of the newborn. Weber observed these movements in 46 out of 54 pregnant women examined by him and they could be found beginning with the 32nd week of pregnancy. Ahlfeld's observations were not in general supported by his contemporaries. In his renewed experiments Ahlfeld was able to demonstrate more clearly than before the existence of intra-uterine respiratory movements. Only a few authors agreed with Ahlfeld (Büttner), while the majority maintained that they had never been able to observe such movements, or that they thought them to be something else, and not respiratory movements (Fromme, Olshausen, Runge). Rrifferscheid renewed Ahlfeld's experiments and came to the same conclusion. In order to throw light upon the question animal experiments have been carried on in the course of the last decades and it was observed that fetuses of different species of animals were not identical with regard to intra-uterine respiration (Windle and Barcroft, Snyder and Rosenfeld, Barcroft, Barcroft and Barron, Bonar et col., Schock, Klemperer). The different sensitivity of different animal species to the activation of intra-uterine respiratory movement has been explained as due to the dissimilar construction of the placenta; those whose placenta

is easily expelled, were thought to begin to breathe during the experiments in consequence of the coming away of the placenta, whereas those whose placenta is firmly adhering, do not begin to breathe, even if the uterine cavity is opened (Heinricius, Engström, Cohnstein and Zuntz). According to Barcroft's researches the age of the sheep fetus has its influence on how easily and due to what reasons it makes respiratory movements. Benecke demonstrated on guinea-pings, Snyder and Rosenfeld on cats and Wislocki on guinea-pigs and cats, that a colour substance injected into the amniotic cavity found its way into the lungs of the fetus whereas Windle and his collaborators came to the conclusion on the basis of examinations made by means of a roentgenography contrast medium, that guinea-pig fetuses did not as a rule aspirate amniotic fluid.

In the course of the last decades and last years workers have attached importance to the intra-uterine respiratory movements and aspiration of the human fetus. American workers have made exact observations of the movements to be noticed in the abdominal wall of pregnant women, and partly compared them to the results obtained by experiment on aminals. Ahlfeld's old conception of the intra-uterine respiratory movements has gained new support (Snyder and Rosenfeld, Bonar et col.). It was also observed that it is possible for the fetus to make respiratory movements already at a very early stage of fetal life (Minkowski, Windle et col.). Dyroff was not able to discern any respiratory movements of the human fetus, when inserting a cystoscope into the amniotic cavity, although he saw the fetus making other movements. It has been possible to demonstrate that an x-ray-contrast medium injected into the amniotic fluid, passed into the lungs of the human fetus (Erhardt, Reifferscheid and Schmiemann, Davis and Potter), but this method of research has also yield negative results (Mugnai and Ingiulla), or it was maintained that the said method of research was not conclusive with regard to intra-uterine respiration (Windle et col.) Aspiration was regarded as due to irritation of the respiratory centre caused by swallowed and absorbed contrast medium (Pischinger). Szendi noticed that already a 3 months old human fetus aspirated colour substance injected intra-uterinally. Indian ink injected into the amniotic cavity did not pass into the

lungs of the human fetus (Pischinger). On the basis of theoretic consideration Walz arrived at the result that intra-uterine respiratory movements are an absolutely necessary condition for the maintenance of the fetal blood circulation, and that they regulate the latter. It seems as if his theory was quite conclusively overthrown (Dyroff, Schmitt). It cannot be considered that the idea of intra-uterine respiratory movements were universally adopted, as it has also been opposed (Eckstein and Rominger, Salmi). Yet Smith (1945) considers this opinion to have become »satisfactorily established».

Mention has already been made of the elder viewpoints regarding aspiration of the amniotic fluid (Röderer, Scheel, Schwartz, Schultze). Böhr found in his post mortem examinations of 57 stillborn or asphyxiated newborn infants that 41 of them had amniotic fluid substances in the lungs — according to macroscopic observations. Ahlfeld supposed that intra-uterine respiratory movement only caused the amniotic fluid to pass as far as the trachea, and Reifferscheid was of the opinion that respiratory movements took place with a closed larynx. Some later authors have adopted the point of view that in the course of intra-uterine life the amniotic fluid is only conveyed as far as the trachea or the mouth (Balthazard and Pièdeliévre), whereas others maintain that if there are intra-uterine respiratory movements, they must also cause an aspiration of the amniotic fluid as far as the lung (Fromme, Schmitt, Peiper). This is connected with the old question as to whether the aspiration of the amniotic fluid is to be regarded as a sign of asphyxia in the fetus (Schwartz) or whether the amniotic fluid can be present in the alveoli also without asphyxia (Schultze). Any special significance is not as a rule attributed to findings of small quantities of amniotic fluid (Hochheim, Johnson and Meyer, Loeschke, Weimann, Snyder and Rosenfeld, Balthazard and Pièdeliévre) — it is however considered that significant quantities of aspirated amniotic fluid are a sympton of asphyxia (Nippe e.a.), while others feel that aspiration is always a sign of anoxia (Windle). Table 1 is meant to illustrate the frequency of occurence of amniotic fluid aspiration according to different authors. Their results cannot be compared forthwith, because their material is not similar, both with regard to the methods em-

ployed and the age at death of the subjects examined. Camerer has one of the most extensive materials, and according to him aspiration has occurred nearly to a hundred percent in infants who died under a week old. — No difference has generally been established as to the quantity of amniotic fluid in different lobes (Camerer, Hochheim).

Several authors consider that a strong aspiration is dangerous (Helwig, Szlavik, Shock, Camerer, Hochheim) and Franzmeyer is of the opinion that aspiration of the amniotic fluid is a complication mostly leading to death. Preyer thinks that the aspiration is rather an indicator of asphyxia than its cause.

The observations made in the researches mentioned in Table 1 are based in a microscopic examination of specimens taken from lungs. Different methods of staining have been proposed in order to demonstrate the presence of amniotic fluid in histologic preparations (Radtke, Strassmann, F. etc.). Several authors have used fat staining in their researches (Hochheim, Camerer, Hook and Katz). Farber and Sweet are of the opinion that hematoxylin and eosin staining makes the liquor amnii substances visible and that it is unnecessary to recur to any other methods. Of the amniotic fluid substances, cornified squamous epithelium cells are considered the most typical, and their presence most common together with fat. Meconium and lanugo hairs are met with more rarely (Camerer, Hintner). No conclusions can be made on the basis of the liquid part of amniotic fluid, because it does not fix owing to its low protein contents (Fraenkel and Weimann, F. Strassmann), or it occurs »as a precipitate and so presents no distinctive picture» (Farber and Sweet) — yet Warwick felt he could establish the presence of amniotic fluid in the lungs solely on the basis of the precipitate, and it was present without any firm particles in 25 % of his cases. Whitehead and his colleagues are of the opinion that the liquid substance found in the lungs is a transudate, and that there is in general no normal aspiration of the amniotic fluid, but to the contrary, a flow from the lungs into the liquor amnii. Kermauner on the other hand considers that the mucus to be found in the respiratory passages is due to irritation of the mucous membranes and Leff thinks that edema due to heart insufficiency is the reason of the circumstance that the lungs of the newborn seem

TABLE 1

Presence of Liquor Amnii Substances in the Lungs According to Post Mortem Material

Author	*Age and number of cases*	*Presence of amniotic fluid*
Hochheim 1903	43, of whom 21 stillborn and remainder newborn	In all
Thaysen 1914	Under 3 days 32 cases	In nearly all
Hook 1927	Under 14 days 54 cases	In 43
Hook and Katz 1928	Under 17 days	Frequent
Loeschke 1928	Stillborn	In all
Lauche 1928	Under 2 days 16 cases	In all cases in the respiratory passages, in 12 cases in the alveoli
Farber and Sweet 1931	Under 6 weeks 124 cases	88 %
Szlavik 1931	Under 9 days 35 cases	In all
Kaldor 1933	Newborn 17	In 13
Murphy and Bauer 1933	60 died under 24 hours age 30 of them treated by respirator	In alveoli in 40 cases
Franzmayer 1934	Under 2 days 61 cases	Cause of death in 31 (with complications)
Warwick 1934	Under 2 weeks 240 cases	73 %
Camerer 1938	Under 1 week 212 cases	In 209
Yamamura 1939	24 cases of newborn and stillborn	In all fullterm infants, in 5 prematures out of 17

to be full with mucus — the amniotic fluid normally present in the trachea does not generate it, nor is aspiration its cause.

It is considered that aspiration of liquor amnii is significant for the development of the lungs. — The opinion has been expressed that aspirated amniotic fluid participates in producing changes in the alveolar epithelium, helping them to become flattened (Ste-

WART). The fat to be met with in the cells of alveolar walls has also been considered to have its source in the amniotic fluid, but possibly to be also of some other origin (HOCHHEIM). SNYDER and ROSENFELD have come to the conclusion that liquor amnii constantly present in the alveoli, causes the apperance of the alveolar lumen in the course of fetal life.

There are not many studies regarding the fate of aspirated amniotic fluid in the alveoli. Of the older authors, SCHEEL was of the opinion that it evaporates and gets absorbed in the infant's lungs. ADDISON and How found in congenital atelectasis »Wanderzellen» in the alveoli of the lungs, whose task it was, according to their conception, to remove the »cellular debris», and the liquor amnii would be rapidly absorbed. The fat was considered to disappear by resorption by way of the alveolar epithelium (HOOK and KATZ) and the cellular particles disappear through the influence of phagocytosis and resorption (HOOK). ERHARDT's x-ray examinations proved that a contrast medium injected into the amniotic sac showed a shadow only 48 to 72 hours afters the injection, which ERHARDT explained as due to the circumstance that aspirated amniotic fluid was absorbed in the lungs, but the contrast medium remained, being incapable of absorption, and by means of repeated aspiration it was by and by concentrated so much that it gave a shadow, which it did not do in the concentration when it was in the amniotic sac. The same observations were made by REIFFERSCHEID and SCHMIEMANN. CAMERER was of the opinion that already during the intrauterine stage the liquid parts of the amniotic fluid are rapidly absorbed, the fat is taken by the »Wanderzellen» and the capillary endothelial cells. The cellular particles of the liquor amnii are »der Alveolarwand angelegt» in infants a few days old, but CAMERER could not say anything as to their later fate. BENECKE is of the opinion, as a result of animal tests, that amniotic fluid is possibly absorbed by way of the lungs, although he was unable to demonstrate this conclusively in his experiments. — Particles of liquor amnii have been found in the lungs of prematures, even a couple of weeks old (LOESCHKE).

As already mentioned, CAMERER found the cellular particles of the amniotic fluid to be »der Wand angelegt». Chiefly American authors have drawn attention to the fact that liquor amnii some-

times forms membranes (Farber and Sweet). Similar membrane formations are also to be found in the adult, mainly in connection with influenza (Opie) but also due to other diseases — in children above all in pneumonia. (Farber and Wilson) Farber and Sweet called the membranes they found in the newborn »v e r n i x m e m b r a n e» or »h y a l i n e m e m b r a n e». Farber and Wilson reported to have found them in 40 cases, and therefore the findings cannot be regarded as anything especially rare. Hochheim (1903) found already in two cases of the 43 newborn he examined in the alveoli a mass which is evidently identical with the membranes described later, and which he considered due to the aspiration of amniotic fluid in the newborn. Hochheim also found, like later authors (Farber et col., Hunt, Ahlström, Johnson and Meyer, Steinharter, Hook and Katz, Baar, MacGregor,) that this mass was present only in infants who had breathed, and considered that it was due to the amniotic fluid being flattened against the alveolar walls. These membranes were found to be free from fatty material only in one case (Steinharter) of all reports on infants. They are stained in the same manner as hyaline (Farber and Wilson etc.) and are free or nearly free from fibrin (Farber and Wilson, Ahlström.) Farber and Wilson produced experimentally similar membranes in animals and came to the conclusion that the chief factor effecting their appearance is an impeded — forced breathing, the result of which is the flattening of the contents of alveoli against the walls. According to their researches, these membranes are composed of disintegrating cells or necrotic tissues. Necroses have not been found in the alveolar walls of the newborn. Fat according to Farber and Wilson is part of the membrane-forming substances, and not come from the blood.

Membranes were found in asphyxial newborn, the more pronounced, the more serious and prolonged the asphyxia (Farber and Sweet). Ahlström considers that the membranes can be a serious obstacle for the exchange of gases, and thereby a cause of death, especially in prematures.

Hochheim (1903) found a substance often present in the lungs of the newborn, blue when stained with hematoxylin in a frozen section, which has been named m y e l i n (Virchow etc.). He

thought that this substance often appeared postmortally, but also *intra vitam*, as a result of aspiration of amniotic fluid. Myelin is formed of desquamating cells of the alveolar epithelium, where it is visible in a hematoxylin stained frozen section »in Form schwarzblauer Tropfen und Schollen». Myelin was found by Hochheim also in the lungs of older infants, where it could no longer be thought that the myelin formation was a result of aspiration.

Myelin is also found in the lungs of the adult, it is possibly a normal result of the excretion of the bronchial epithelium (Panizza, Schmidt), which are met with in expectorations as small granules (Schultze). — According to Kawamura, myelin in the lungs of the newborn is mainly »wohl sicher ein postmortales Produkt», whereas Aschoff considers that changes in the alveolar epithelium take place intravitally »unter dem Bilde von Myelinisation». Szlavik found myelin in the lungs of all the newborn he examined, nor was its quantity depending on the abundance of the aspirated amniotic fluid. He thinks that myelin present in the alveolar lumen shows that the alveoli were not aerated, and differentiates between congenital and secondary atelectasis on the basis of the presence of myelin. Weimann found that myelin appeared in decayed lungs of the newborn and in the cases of Hook and Katz myelin was more often found in those, where more time had elapsed between death and autopsy. It appears therefore that it is not possible to come to reliable conclusions on the basis of the presence of myelin in post mortem material.

As may be noted from the above survey of literature, there are still some divergencies of opinion and questions in need of elucidation with regard to the researches on lungs of the newborn. I therefore feel that my investigation is justified.

II Material and Methods

The material has been collected at the I and II Women's Clinic of the University, Helsinki (N I and N II), at the Midwives College (K) and the Childrens Clinic of the University, Helsinki (L). Part of the autopsies has been carried out at the Patho-Anatomic Institute of the University, Helsinki (P). These were cases treated at the Childrens Clinic. With few exceptions, I have carried out the post mortem examinations myself, and made complete autopsies according to the method employed by the ZENKER school. I have tried to make the post mortem examination as soon as possible, and it has generally been carried out within less than 24 hours, in some cases in 1 to 2 hours after death. It must be admitted that some of my cases showed post-mortal changes that interfered with the estimation of my results, but by comparing to each other cases on which the outopsy was performed at different times after death, I feel it has been possible to estimate to a certain degree what changes are to be considered as appeared *intra vitam*. The lungs were removed in toto together with the organs of the throat and the thoracic cavity and placed whole into a 10 % solution of formaldehyde. After the fixation of the lungs in toto, pieces were dissected from each lobe, and in addition from the lingula. The pieces were subjected to fixation for a time of 24 hours in a 10 % solution of formaldehyde, after which they were embedded in paraffin, using chloroform as clearing medium.

The trachea was not ligatured before opening. It was not possible to fix the lungs in situ. It cannot be denied that this post mortem technique used by me can cause changes in the dilatation of the lungs, and it is even possible that the effect is not similar in all cases. In my experience, it is of no special significance to ligature the trachea of the newborn, because if one ligatures the trachea and unties it after the opening of the thoracic cavity, a hardly noticeable collapse of the lungs takes place, and in some cases no change can be noted. In the animal experiments, where a quantitative comparison of the size of the pulmonary lumina was made, I have tied off the trachea.

Paraffin sections of 5 μ in thickness were stained with WEIGERT's hematoxylin and VAN GIESON, DELAFIELD's hematoxylin and eosin, and orcein (1 per cent solution in 70 per cent alcohol with Hcl) Part has in addition been stained by REGAUD's hematoxylin and MASSON's acid fuchsin-aniline blue and by HARRIS' hematoxylin and MAYER's mucicarmine. In some cases the sections fixed in CARNOY's fluid were stained by BEST's carmine, using EHRLICH's acid hematoxylin for staining the nuclei. In order to obtain a general idea, 30 μ, 60 μ and 120 μ thick paraffin sections were stained with DELAFIELD's hematoxylin and eosin. The frozen sections taken from the formalin fixed lungs, both upper and lower lobes, were stained with ROMEIS' colloidal sudan-orange or with scharlach-R (KRAJIAN's modification), or both methods were used. For staining the nuclei in these sections DELAFIELD's or HARRIS' hematoxylin were used. Part of the frozen sections was stained in addition by Nile blue sulphate and the LIEBERMANN-BURCHARD-SCHULTZE reaction was carried out.

The frozen sections were also stained with HOYER's thionine stain. In addition, such other staining methods as were considered necessary were applied in different cases. WEIGERT's hematoxylin and V. GIESON and DELAFIELD's hematoxylin and eosin stainings were in as a rule sufficient to give a general picture, and I consider that other stainings were of great assistance only for analysing the alveolar contents. When staining fat, sudan was especially good to produce a intensive coloration, both with regard to fat revealed in the lumina and the inner fat in cells. On the other hand, the Nile blue sulphate produced a much weaker staining and did not by far reveal the relation of fat to the cells equally well as was the case in the sudan and scharlach-R sections.

I have tried to exclude from my material all macerated subjects and such who had had clearly visible inflammatory changes in the respiratory passages. I have considered such of my cases free from inflammation, where my sections did not show accumulations of inflammatory cells, either in the lumina or in the walls. The presence of a few granulocytes was not considered sufficient to exclude the case. Partly due to the reason that it was difficult to collect enough material free from inflammation, I have been constrained to include some such cases where there were some restricted inflammatory changes. Moreover, all such cases that were affected with syphilis, either found out clinically or by post mortem examinations, have been omitted. — Hepatic changes may be regarded as some kind of a criterion of possible syphilitic changes in the infant, because they appear in abt. 70 to 80 percent of congenital syphilis cases (THOMSON). Therefore pieces taken from the liver have been examined microscopically in order to ascertain the microscopic changes.

I have considered the age of one month as the upper age limit of the cases in my material. The downward limit was set at 600 gm weight at birth. The majority of the cases are under 10 days old. For the sake of comparison I have also examined older infants. The material comprises in all 95 cases, from stillborn up to half a year old infants. The division of the material into premature and fullterm infants is revealed by the discussion of the cases. According to the now generally adopted determination of YLPPÖ, I have regarded as premature such babies as weighed at birth < 2.500 gm. In conformity with the opinion proposed of late, I have placed into a separate group immature babies who had a birth weight < 1.250 gm (v. NUMERS, YLPPÖ, HENDERSON).*)

In addition to the above material I have also had at my disposal the observations I made at post mortem examinations of infants of different age, as well as microscopic preparations from them, stained with WEIGERT's hematoxylin and VAN GIESON, or with DELAFIELD's hematoxylin and eosin.

The clinical data regarding the cases was obtained from the case or delivery histories. Some infants treated at the Childrens Clinic I have been able to observe from a few hours old until their death.

To complete my post mortem material, I have also carried out several animal experiments. This material is dealt with in a different chapter.

To determine the shape and staining of the liquor amnii substances, films were made from amniotic fluid taken from an undamaged amniotic sac; these films were stained by WEIGERT's hematoxylin and VAN GIESON and by DELAFIELD's hematoxylin and eosin, as well as by ROMEIS' colloidal sudan-orange. In the films thus stained it was possible to distinguish large nuclear cells as well as squamae without nuclei. These presented a similar appearance as the squamae and cells in bits of skin taken from newborn infants. There were also some smears that did not contain more than some single cell and squama, and in addition to them only a precipitate. Even if it appears clear on the basis of the above that amniotic fluid can chiefly appear as a precipitate in the sections, yet I have not regarded the presence of this substance to be a conclusive proof of the presence of amniotic fluid, unless there were other unmistakable reasons for such a supposition.

Calculations were made using the net ocular both on the basis of human post mortem and animal material, how high was the percentage of the area free from parenchyma in both materials, as compared to the total area. The net ocular had 340 squares, and a 300-

*) I am using below "premature" to designate as a group denomination both premature and immature babies, unless it is clear from the context that only that group is meant, whose birth weight is 1250—2499 gm.

magnification was used. When calculating, the areas were chosen in such a way that they were not taken into consideration if they showed lumina that might be interpreted as bronchi or bronchioli, but the section was moved until they disappeared from the field. In this way, at least 15 fields were counted in each section, but if some items showed considerable differences more fields were counted, and it was then attempted to count different areas separately. By using this method of calculation one does not obtain the »actual» size of the lumina, the result only showing their relative proportion. Notwithstanding this, the methods allows of a better comparison of the different cases to each other, than by only measuring with the eye.

III Experimental Investigations

Material and Methods. — The experiments were made on kittens, of which I had 10 litter at my disposal. For some a cesarean section was performed at the end of the estimated pregnancy, some were born spontaneusly. When performing the cesarean section, the cat was anesthetised with choloroform, subsequent to having received morphine 0,04—0,06 subcutaneously. The kittens were weighed immediately after birth. In all these cases, with the exception of the first-born litter, the trachea was tied off before opening the thoracic cavity. After an examination of the lungs in situ, the whole animal was immersed in a fixative solution; in the majority of the tests a 10 % solution of formaldehyde was used as such, and in some cases susa solution (Litters No. 3, 4).

Some hours later the organs of the thoracic cavity were removed and immersed whole in the fixative, the trachea still being tied up. As soon as it was seen that the fixation had taken place, pieces were taken from both sides, both from the upper and lower part, always endeavouring with the utmost possible precision to take pieces from corresponding places. The pieces were embedded in paraffin in the usual way, employing chloroform as clearing medium. 5 μ thick sections were cut and stained with WEIGERT's hematoxylin and van GIESON and DELAFIELD's haematoxylin and eosin as well as orcein. Some serial sections were made and stained in the above way. In addition, some 30 μ, 60 μ and 120 μ thick sections were cut and stained with DELAFIELD's hematoxylin and eosin.

In the cases of the cesarean sections as well as in some spontaneous deliveries it was possible to exactly determine the time of birth, but in some cases it could be established only with the precision of hours. These circumstances will be elucidated in the tables. In order to provoke the appearance of secondary atelectasis the following method was used: the kitten was allowed to breathe oxygen for a time of about 10 minutes. After that curare was administered to it (intraperitoneally 0,1—0,5 c.c. of a 1 percent solution), and the animal was left to inhale oxygen until it died. In these experiments respiratory activity ceased before the heart stopped.

The latter's function became gradually slower. These kittens were treated after death in the same way as explained above. The lumen ration in 5 μ thick sections was calculated according to the method set forth on p. 29. The results of these proceedings are illustrated by tables 2, 3, 4.

Observations

Lungs with Congenital Atelectasis. — These researches were made by studying the lungs of 5 kittens in all. Three of them were killed intra-uterinally, without ever having been allowed to inhale air (Kittens 1/II, 3/II and 11/I), one was made to inhale a little air (7/III) and one kitten died of »intra-uterine asphyxia» in such a way that it was placed into formalin enclosed by the uterus (10/II). The three first ones show a more or less equal expansion (see table 2), although it is different in different lobes. This cannot be measured by the eye, but is only revealed by counting.

TABLE 2

Kittens Killed in Utero

No. of kitten	Lumen ratio (%)				
	I	*II*	*III*	*IV*	*Average*
1/II	45	46	45	37	43
3/II	44	49	43	52	47
7/III	60	63	53	61	59
11/I	50	43	36	41	43
10/II	52	60	72	62	62

The numbers signify: I upper part of right lung, II lower part of right lung, III upper part of left lung, IV lower part of left lung.

The structure of the lungs of kitten 11/I was as follows: *Macroscopically:* the lung is of a light red colour, with a soft consistence, most like to that of a gland. The surface of the lung is of an even colour. *Microscopically:* all the lobes present a similar picture. (Fig. 1) Lumina are clearly discernible everywhere, the tissue looks »nice» and regular. The walls are winding, but the walls in general are not too thick; they make a thicker impression than »in reality», owing to their strongly intricate course. The elastic fibres are wind-

ing, »flabby». In the thin places the walls only have a thin fibre, or there is a single cell adhering, or a capillary springs up from it. The epithelial cells *) lining the walls can be clearly distinguished from the other parts of the walls, and hang sometimes like grapes or berries from their thin central parts. There are one or two cells — very seldom more (3—4) in one place. Their nucleus is of the size of a erythrocyte, round or elliptic. Protoplasma forms a smaller part of the cell than the nucleus. The shape of the cells varies from low prismatic to high prismatic. So e.g. there is a wall near the pleura (under it) that has three highprismatic cells, then a capillary and again two isolated cells with a capillary between them — these cells are isoprismatic. The same variation in the shape of the cells down to the lowprismatic form is seen in different places of the section. In addition to epithelial cells, the walls have capillaries whose endothelial cells have narrow fusiform nuclei. The share of the capillaries is about half the wall. They do not have any unbroken arrangement in the walls on larger areas than what corresponds to the width of 2—3 epithelial cells. In addition to them, the central parts of the walls have cells with fusiform nuclei. In the lumen isolated epithelial cells are demonstrable, which are vaculated.There is also some angular shape without a nucleus that stains a light yellow with Wiegert's hematoxylin and van Gieson, and light red with Delafield's hematoxylin and eosin. Some erythrocytes are seen, and sometimes a precipitate. The lumen is mainly empty. Two nuclei are seen sometimes in the cells situated in the lumen. Kitten 1/II presents a practically similar picture, but the cells can be better distinguished from each other. Kitten 3/II is also similar.

These cases show here and there small areas that only consist of cells — the wall appears thicker, but it is then a place where the lumen has been cut tangentially, so that the »bottom» or the »ceiling» become visible. This impression is gained when examining 30 μ and 60 μ thick sections. Such forms where the lumen is encircled by an unbroken regular ring of cells, are not to be found in the sections.

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*) I am using here and below the name of epithelial cells when referring to cells covering the walls for greater clearness, meaning the cells lining the walls and morphologically resembling epithelial cells.

The lungs of the kitten 10/II asphyxiated intra-uterinally are macroscopically unmistakably larger than those of the preceding cases, and according to calculations made on the basis of microscopic sections, the lumina occypy a visibly greater part than above. Some places show variations within about similar limits as in the forementioned cases. The microscopic examinations also show at once a much greater extension of the lumina, but in other respects the microscopic picture of the lungs does not differ much from the above. (Fig. 2) The walls are straighter, but have no proper »tension». The cells seem to lie at greater distances from each other. Their shapes are identical with those described above. No visible difference can be established in the relation of the epithelial cells to the connective tissue. The number and blood-contain of capillaries are about the same as in other cases of intra-uterine death. This being so, there is no evident difference but in the size of the lumina. The picture as a whole reminds of other cases of intra-uterine death, and diverges from the microscopic picture of lungs that have breathed to such an extent, that it must be placed into the preceding group, in spite of the noticeably larger lumina. The alveolar region does not have any contents worth mentioning, to the contrary, there is less of it than in other cases of intra-uterine death, but instead there are in several bronchi quite a number of the angular formations described above, staining a light colour (amniotic fluid).

The lumina are of about the same extension in the case which was allowed to breathe some air through the torn trachea (kitten 7/III, Fig 3). In this case the calculations did not show the difference between the expansion in different lobes to be greater than in lungs that had not breathed, but when examining microscopically tissue sections, it is seen that some sections have areas of a different character. Here the walls are somewhat more »tense» than in lungs with congenital atelectasis, the difference being yet very little — in point of fact so small that it would be impossible with certitude to transfer it into the air-breathed group. The shape and arrangement of the cells and their relation to the other parts of the walls do not differ greatly from those described above. In some places the cells are not distinguishable so clearly, giving the impression of being pressed against the walls. These latter appear somewhat thicker than in the lungs of other cases with congenital atelectasis. With

regard to its weight, this kitten was somewhat more removed from a fullterm animal than those dealt with above.

Aerated Lungs. — My material comprises in all 29 kittens who had breathed air. Attempts were made to affect 10 of them with secondary atelectasis – I am dealing later with these cases. Nineteen kittens were allowed to breathe freely. They were killed at different ages — at the utmost two days old, and one of them died.

Aerated lungs are already macroscopically easily distinguishable from the lungs of those who had died intra-uterinally, as described above. They are unmistakably more expanded, of a light colour, and showing on the surface transparent aircontaining lumina. The microscopic picture (Fig. 4, 5, 6, 7) is also quite different from the one presented by the animals described above, who had died intra-uterinally: the walls are straight, "tense" — they look thinner and the number of capillaries is smaller (in other words, the capillaries contain less blood) than in animals who had died in utero. The elastic fibres are tense. In addition, it can be seen in thin sections (5 μ) as a difference from animals with intra-uterine death, that the contours of the lumina are straighter — the irregularities that are due to the epithelial cells and capillaries rising from the walls, are absent in these sections. Epithelial cells are few, and clearly distinguishable only in the corners. In these places and in thick sections there are alveolar lining cells with a shape that is strongly reminiscent of the cell shapes seen in the lungs of animals who had died in utero. I have been unable to find any alterations in the forms of the cells in these sections, on the basis of which it would be possible to discriminate between a lung that has breathed and a lung of an animal who has died intra-uterinally.

I do not feel I can, on the basis of the staining methods employed by me, go into the widely discussed question as to whether respiration causes changes to appear in the cells of the alveolar lining, and as to what is the cause of the difference between the alveolar walls of a fullterm fetus and a newborn animal who has breathed. The purpose of my study has been in the first place to clear up the difference between the pulmonary structure of lungs with congenital and secondary atelectasis. As this difference, according to my opinion, is better illustrated by the general pulmonary picture than by

the form of individual cells, a study of the changes in the latter seems to be less appropriate in this connection. In such places where it was possible to study these changes (corners of the thin sections and the 30 μ—60 μ sections) I have been unable to determine any difference in shape suitable for this differentiation.

Lungs with Secondary Atelectasis. — As already mentioned above, I have attempted in ten cases in all to provoke secondary atelectasis in the lungs of newborn kittens. In some of them it was possible to render the lungs macroscopically entirely airless. Microscopically spaces could be found also in sections made from such lungs — and upon counting the ratio of spaces appearing in the whole area of the section, it was found that it was more than 10 % of the area, although there were places in the section that were entirely devoid of lumina.

The lumina of the lungs that appeared atelectatic on the surface were on an average unmistakable smaller than in the lungs of animals where respiration had taken place and that were killed suddenly. It is justified to consider these lungs at least partially atelectatic, and on the basis of the picture presented by them, to estimate the difference between congenital and secondary atelectasis of the lungs.

As already said, the sections showed areas where no lumina could be distinguished at all. Such areas can therefore be regarded as completely atelectatic. They are unmistakably of a different construction than the lungs of animals killed in utero, already on the basis of the general picture presented by the section (Fig. 8). The tissue is compact, irregular, and cannot easily be recognised as lung tissue. There are variations in the form of the cells, but it is impossible to establish any fundamental difference as compared to the lungs of animals killed intrauterinally. In these places it is difficult or impossible to distinguish the epithelial cells from other cells of the wall (see Fig 9). There are better possibilities to study the structure of the walls in those places where there is a small slitlike lumen (Fig. 10). The walls are thicker in comparison to those in the lungs of fetuses killed in utero. The whole structure is coarser, the lumina do not have as many partitions as in the lungs of these latter. The epithelial cells are not as clearly distinguishable as those rising isolated in the lumen, but they are »pressed» against each

other, forming in this way together with the capillaries a uniform lining of the walls. When studying thick sections, it is seen that the lumina look slitlike, in contradistinction to those of a regular round shape in the animals killed intra-uterinally. The corresponding places of the sections taken from the lungs of kittens of the same litter show a great number of small, round or oval lumina in the lungs of animals who died in utero, whereas in lungs affected with secondary atelectasis the lumina are slit-like and much fewer in number. I do not feel that it is possible to distinguish these lungs from those of animals killed in utero on the basis of the forms of epithelial cells.

Attempts were made to affect the kitten 7/IV with secondary atelectasis at the age of 4 hours. The animal was premature, weight at birth being 75 gm. Its breathing had been weak and rattling the whole time. The conditions under which the experiment was made and its course were similar to the other cases. The lungs did not become completely atelectatic, but it was possible to distinguish macroscopically areas that were unmistakably air-containing. The left lung presented macroscopically and microscopically an appearance of congenital atelectasis and lumina were clearly seen everywhere. A section taken from the right lung showed some lumina with arched »tense» walls, where the cells could not be seen clearly. The experiment speaks on behalf of the supposition that the lung, in order to become atelectatic in a secondary manner, must first be aerated — i.e. that the alveoli do not collapse unless some air had entered them first. In the animals of the same litter that had a longer life (7/I and 7/II) atelectasis could be macroscopically determined everywhere in the lungs, and the shape of their walls and lumina was microscopically different from congenital atelectasis. In the lively kitten (5/III), which was subjected to the oxygen-curare treatment when 2 hours old, the lungs became macroscopically airless and the structure differed microscopically from congenital atelectasis. The lumina were comparatively larger than in the kittens 7/I, 7/II and 4/II, which were older when subjected to treatment.

Discussion

As stated at the beginning of the chapter, the lumen ratio in the lungs was counted. The results of these counts are illustrated by tables 2, 3, 4.

TABLE 3

Kittens in whom Respiration had Occured

No. of kitten	*Age.*	Lumen ratio (%)				
		I	*II*	*III*	*IV*	*Average*
1/III	2 ½ hours	45	53	30	40	42
1/IV	54 hours	56	40	57	61	52
4/III	1 ½ days	53	61	50	58	56
5/I	25 hours	52	50	52	47	50
5/II	53 hours	44	54	47	42	47
5/IV	2 hours	57	53	59	50	55
6/I	1 hour	46	43	44	42	44
6/II	20 min.	62	53	70	53	60
8/I	2 hours	66	66	58	56	62
8/II	42 „	77	77	69	77	75
8/IV	20 „	57	57	51	46	53
9/I	2 days	54	45	56	45	50
9/II	2 „	35	54	46	72	52
9/III	2 „	49	69	57	83	65
9/IV	2 „	75	81	42	41	60
11/II	45 min.	91	79	85	73	82
11/III	10 „	47	49	50	58	51
11/IV	10 „	74	54	75	55	65

The numbers signify: I upper part of right lung, II lower part of right lung, III upper part of left lung, IV lower part of left lung.

In the lungs of the animals killed intra-uterinally the lumina in the different cases belonged to about the same class of size in the kittens 1/II, 3/II and 11/I. These animals were killed in the same way by squeezing the trachea while the fetus was within the amniotic sac. They were not seen to breathe and neither macroscopically nor microscopically could any areas be found that might be considered having become aerated. In this respect the lungs are congenitally atelectatic. The fetuses did not, while they were visible, aspirate any amniotic fluid in the uterus. The other animals of the same litter did not begin breathing immediately after birth, but remained in a state of apnoea for a few minutes. In each case the mother had received morphine and been anesthetised with chloroform, which may have partly been the reason why the kittens were

TABLE 4

Kittens Treated with Curare and Oxygen

No. of kitten	*Age.*	Lumen ratio (%)				
		I	*II*	*III*	*IV*	*Average*
1/V	49 hours	26	31	24	34	29
4/I	1 ½ days	41	47	31	39	39*)
4/II	1 ½ „	17	20	19	17	18
5/III	3 h.45min.	30	31	32	34	32
7/I	77 hours	24	22	21	25	23
7/II	23 „	28	18	14	18	20
7/IV	6 h.20min.	40	37	43	43	41

The numbers signify: I upper part of right lung, II lower part of right lung, III upper part of left lung, IV lower part of left lung.

not active. It can therefore be said that there evidently had not been any extension of the lumina in the lungs after the cesarean section was begun. It is impossible to say whether the fetuses had made intra-uterine respiratory movements when the anesthetic first took effect, and whether this may have modified the »normal» intra-uterine state of their lungs. I feel however it can be indisputable affirmed that the lungs were congenitally atelectatic in all these cases, according to the general interpretation of this concept. Even if the microscopic picture of the lungs does not in every way fulfil all those demands which have been laid down for congenital atelectasis of the lungs. (See p. 14).

Fetus 10/II suffocated in utero without ever having breathed air. Its lungs did not otherwise differ from those described above, but for their unmistakably larger size, even macroscopically. Microscopically their lumina were quite evidently more extended than in the three previous fetuses, and when counting the ratio of the lumina, it was possible to ascertain that the ratio was much higher than for the others. If this case is set apart from the others without considering it any more as congenitally atelectatic, one arrives at the result that the lungs of a fetus that had died intra-uterinally

*) only curare

and not inhaled air, are not necessarily congenitally atelectatic. It is evident that when the fetus dies in utero, factors often occur that constrain it to aspirate amniotic fluid, even in considerable amounts. If they are removed from the group of congenital atelectasis, this may often cause still greater confusion with regard to some individual cases, as to whether a certain case should be considered congenitally atelectatic or not. The easiest course therefore would be to regard such cases also as congenitally atelectatic, irrespective of the extension of the lumina. This latter should then be left out of the determination of congenital atelectasis (in so far as it is wanted to make this determination on the basis of the histologic picture). I shall revert to this question with regard to the human fetus in the chapter dealing with human post mortem material.

In the lungs of such kittens who were allowed to breathe air but were killed suddenly, the size of the lumina was subject to great variations in individual cases. There are also sometimes greater variations in the different lobes of the same case than what is seen in different places of congenitally atelectatic lungs. These variations in size are noticeable also in such cases where the lungs appear fully aerated macroscopically, nor are there any atelectatic areas to be found microscopically. The lumen ratio in the lungs of the kittens belonging to the same litter but killed in different ways (kittens 9/I—9/IV) varied considerably. If it is taken into consideration that already in lungs with congenital atelectasis the lumen extension can be 40—60 per cent of the whole area in microscopic sections, it is evident that it is impossible to determine the aeration of the lungs only on the basis of the size of the lumina — or at least, it is impossible to say whether some area is air-containing or not. It also appears evident that the different kittens cannot be compared to each other on the basis of such calculations. A comparison of the lumen sizes of kittens 8/I—8/IV speaks for the supposition that the lumen ratio grows in the course of the first 24 hours. Yet the material is so small that it does not allow of any conclusions if the differences are not more considerable than those illustrated by the tables. A better idea of the aeration of the lungs than a simple counting of the size of the lumina, is a microscopic study as to whether the lungs show any atelectatic areas. Having made a discrimination on the above principles between congenitally

atelectatic and air-containing areas, it was found that the lungs of a kitten less than one hour old can already be free from congenital atelectasis. The congenitally atelectatic areas persisted for the longest time in the regions of the large bronchi, as the said areas were most often to be found in these places.

There were great variations in the extension of the lumina in lungs affected with secondary atelectasis by means of oxygen inhalation and curare. Not a single time was it possible to achieve a complete absence of lumina in the whole area of the lung. While the lung appeared macroscopically airless, tough, of a dark greyish-red colour, spaces were clearly seen in the microscopic section. The lumen ratio averaged about 20 % in these cases. According to these counts, the lumen was unmistakably less extended than in the lungs with congenital atelectasis. Even if there were completely airless areas in the lungs whit secondary atelectasis, and one can therefore say that complete atelectasis is possible, — yet it cannot be denied that in these cases such areas are also atelectatic where narrow spaces are found in the tissue. The borderline between atelectatic and non-atelectatic is not clearly defined here. I do not find it indicated, or even possible, on the basis of this material comprising only newborn kittens and secondary atelectasis originated only in one way, — to go into the question of atelectasis appearing in a secondary manner, or to attempt a general determination of it. In such cases that were airless (atelectatic) macroscopically, the extension of the lumina was 20—30 per cent of the section area. The lumen ratio clearly surpassed that percentage in the cases that showed macroscopically aerated areas (Kitten 4/I). — It is possible that the lumen ratio is different in different species of animals, therefore conclusions can be made on the basis of the above only in so far as newborn kittens are concerned.

Conclusions

Kittens that are not allowed to breathe air and whose lungs are macroscopically airless, show unmistakable lumina over the whole pulmonary area, their ratio amounting to about half of the latter. If the kitten had strongly aspirated intra-uterinally, the lumina were considerably more extended, but the lung still retained a construction reminding of congenital atelectasis.

At the onset of respiration changes take place in the lungs of the kittens, not only in the shape or extension of the lumina, but the structure of the walls also alters. It is not considered possible in this paper to differentiate on the basis of the forms of the cells between initial (congenital)and secondary atelectasis.

It is possible to distinguish secondary atelectasis in kittens from the fetal condition of the lungs, as well as on the basis of macroscopic and microscopic characteristics. In lungs affected with secondary atelectasis the lumina are smaller than in the airless lungs of a kitten dead at the time of birth. Microscopically a difference is seen both in the shape of the lumina and the position of the cells on the walls.

IV Human Post Mortem Investigations

1. Congenital Atelectasis and Aeration of the Lungs

Fullterm Infants

Stillborn and Asphyxiated who did not Resuscitate. Congenital Atelectasis

There were 14 *stillborn infants* according to the delivery histories. It cannot be considered *a priori* that the lungs of stillborn infants are the same as in the fetal state. I.e., they are not a suitable starting-point for a research as a type of lung where no respiration has occurred. There are numerous observations as to how stillborn babies — even fetuses taken out of undamaged amniotic sacs — both macroscopically and microscopically show air-containing areas in their lungs (Lados, Kathe, Hofmeier, Dürig, Raestrup, Meixner, Schönberg, Strassmann, Hecker, Wille).

Of the stillborn babies of my material one died during pregnancy and the others in the course of the delivery. Of those who died during delivery five were such (cases no. N 2143/I/44, N 906/I/46 A, K 719/45, K 1811/45 and K 643/46), in whose lungs it was possible to find already macroscopically air-containing areas on the surface of the lungs, differing from the pulmonary tissue elsewhere. Nine others were more or less similar to each other. Their lungs were tough, resembling glands in their consistence, the surface was smooth,regular,the colour varying between greyisch-red and greyish-purple. The lungs sank in formalin.

The only case of my material who *died in the course of pregnancy* (N 626/I/45) had small, greyishpurple lungs. The following was found by means of a microscopic examination of them: The epithelial lining of the bronchi and bronchioli had come off in small patches everywhere and filled their lumina. The main

part of the tissue of the alveolar tree was formed by engorged capillaries. The endothelial cells in the capillaries were clearly visible, their nuclei were crescentshaped, well stained. There were but few cells in the alveolar epithelium - they were generally detached in the lumen. Only some cells adhered to the walls. Their shape was isoprismatic, sometimes somewhat higher, sometimes somewhat lower. The form was often irregular and the protoplasma indistinctly visible. The nucleus was round or elliptic, well stained. The cells in the connective tissue of the walls were well preserved. The shape of the nuclei in the cells of the connective tissue was fusiform, the nucleus often arched, its length about 3—4 times larger than its thickness. Long and narrow nuclei were nowhere visible in the cells of the connective tissue.

The case was not a good one, in so far as the postmortal changes were already far developed, but such changes are so rapid in babies who die during pregnancy, that they are already present at birth. The post-mortal changes were even more advanced in other infants dead during pregnancy whom I have examined, and their tissue structure was entirely blurred.

In case N 2246/II/45 there was a striking engorgement of the blood vessels in the histologic section. There was a clear preponderance of capillaries in the walls, and also touching the lumen nearly exclusively engorged capillaries. Their endothelial cells had crescent-shaped or fusiform nuclei. The walls ran a tortuous course and the capillaries bulged out into the lumen. The alveolar epithelial cells were usually single in each place, but in some places 2—3 close to each other. They were iso- or lowprismatic, the nucleus was round and well stained, lying in the centre of the cell or somewhat basally. Protoplasma was slightly stained, taking up half the cell at the utmost. Sometimes the cells in the capillaries can misleadingly resemble epithelial cells, but it is possible to make the distinction on the basis of the shape and situation of the cells. Cells resembling those of the alveolar epithelium were found detached in the lumen. In such cases their protoplasma was granulated - - some cells were clearly disintegrating. The nuclei in the cells of the connective tissue of the walls were fusiform, their length surpassing their thickness 2—4 times. The bronchial epithelium was well preserved and stained strongly. Thus, there are no essential differences between this case

and those who had died in utero, the differences having probably been produced by the abovementioned post-mortal changes.

The highest lumen ratio was found in cases N 2686/II/45 and N 810/II/45 (see table 5). Their microscopic picture does not greatly differ from the preceding. The lumina appeared here more extended and the walls thinner than above. The amount of blood in the capillaries was evidently less than in those with smaller lumina. There were also in these cases clearly discernible highprismatic epithelial cells, although the lowprismatic were perhaps the majority. Practically every lumen had contents, although they did not fill them completely in the section. I shall make a more detailed report on these contents in the chapter dealing with aspiration of the amniotic fluid.

In the other cases no essential differences in structure could be found microscopically, except variations in the size of the lumina. (Table 5 gives an idea of these variations. See also Fig. 11, 12,13)

TABLE 5

Lumen Ratio in Stillborn Fullterm Human Fetuses

No.	*I*	*III*	*Average*
N 626/II/45	17 % ?	—	17 % ?
N 2659/II/45	15 %	15 %	15 %
N 1634/I/45	36 %	33 %	34,5 %
N 810/II/45	47 %	47 %	47 %
N 847/II/41	31 %	29 %	30 %
N 965/II/41	30 %	29/%	29,5 %
N 2246/II/45	20 %	19 %	19,5 %
N 2686/II/45	38 %	39 %	38,5 %

Th numbers signify: I right upper lobe III right lower lobe

In case N 2143/I/44 the fetus died evidently due to the prolapse of the umbilical cord. Macroscopically there was a scant quantity of air in both upper lobes. It is possible that it had entered the lungs in consequence of the insufflation recurred to. Microscopically the picture was in several sections similar to that described in the above cases. But there were some places where

the walls seemed straighter, more taut, the lumen was empty. In such places there was no twisting of the capillaries, they did not rise into the lumen in the same way as in airless places. There was not any considerable difference in the thickness of the walls, nor in the shape of the epithelial cells. The nuclei of the cells in the connective tissue were oblong in some places, but the difference was not distinct as compared to the airless area.

In case K 643/46 there were no essential differences in the structure of the aerated areas compared to the above, although there were more air-containing areas and they were more widely spread. The walls were thick in part of the area. But in several places they were thinner than in the previous case. The epithelial cells were high-, iso- or lowprismatic also in the areas with extended lumina. It could not be found that the cells in these areas were lower than in the airless places. The capillaries were less full of blood and flush with the walls; they did not have a winding course. In some places the nuclei of the mesenchymal cells were elongated into a narrow ribbon-like shape, but this was not the case everywhere.

In case K 719/45 the lungs were nearly everywhere aerated, of a light colour, the pieces cut from them floated. Microscopically the alveoli were wide open, their walls thin, sometimes »thread-like». (Fig. 14) The tissue had but little blood, the capillaries were thin. Alveolar epithelial cells were isoprismatic, they could be clearly seen in the angles of the extended lumina, but sometimes some isolated isoprismatic cell could be found also on a straight part of the wall. In the walls the nuclei of the connective tissue cells were often long and narrow, unmistakably narrower than in the airless area. However, there were also fusiform nuclei that looked like mesenchymal cells. The histologic picture of aerated areas in the other cases did not present any aspects essentially differing from what has been already described.

There are only 4 cases who, according to the delivery histories, were born *asphyxiated and did not resuscitate*. One of them had aerated areas both macroscopically and microscopically (case N 979/I/46). The microscopic picture was similar to what has been said above with regard to insignificantly aerated lungs. (e.g. case K 643/46). The microscopic picture presented by the others was such as

has been described above for airless lungs, the size of the lumina varying also from case to case.

Thus, these cases are not essentially different from those who had died in the course of the delivery.

The structure of the lungs with congenital atelelectasis on the basis of the cases described above is as follows:

The different lobes of the lungs present the same picture. Unmistakable lumina are to be found everywhere. In other words, the walls are not in close contact to each other. The walls are tortuous, their thickness varies in different cases. It can often be noted that the relation between the thickness of the walls and engorgement of the capillaries, and on the other hand the extension of the lumina, is inversely proportional. The alveolar epithelial cells are high-, iso- or lowprismatic, irrrespective of the size of the lumen. The mesenchymal lining cells are fusiform, their nuclei lie in the same direction as the course of the walls or slightly diverge from it. The thickness of the nuclei surpasses their length from 2 to 4 times. The nuclei in the capillary endothelial cells are twice to 4 times as long as thick, fusiform or crescent-shaped. The general aspect is intricate, with numerous compartments. The lumina have contents. — It is evident that these areas are congenitally atelectatic and clearly distinguishable from areas where respiration has occured.

The pulmonary structure of infants who had breathed during delivery has undergone the following changes: the tortuous course of the walls has disappeared. It appears as if the bulging capillaries and cells which caused the irregularity of the lining surface, were partly drawn into the wall. No essential changes can be noted in the shape of the alveolar epithelial cells, as there are high-, iso- and lowprismatic cells also in aerated lungs. The shape of the nuclei in the mesenchymal cells has sometimes undergone changes. They are narrower and longer than in lungs with congenital atelectasis. The capillary endothelial cells are perhaps somewhat narrower in aerated than in congenitally atelectatic lungs. Both these nuclei and those of mesenchymal cells show similar forms as in congenital atelectasis. The general aspect of the lungs has become less complicated, the walls being tense and their irregularities gone. Although it seems that alveolar epithelial cells occur less frequently than in congenital

atelectasis, this is a phenomenon that is probably due to the stretching of the walls. Thick (60—120 μ) sections show a great number of isoprismatic lining cells also in aerated lungs.

Alveolar contents are one of the important distinctive features of congenitally atelectatic lungs. Even if I do not in this connection make a more detailed study of the character of these contents, it is imperative to give a short exposition. Each of the preceding cases where no alveoli expanded by air were determined histologically, had alveolar contents. They do not always fill the whole lumen, but appear as precipitate, usually in its central part. Extended lumina are partly empty, but smaller lumina seem to be completely filled with the substance. This is not clearly visible in aerated lumina, and if there is some residue, it is found along the walls of the lumina. In addition to the forementoined substance, pieces can often be found which are skin epithelium cells or vernix caseosa. Their precense is not equally regular and their number greatly varies in different cases.

The microscopic picture of non-aerated lungs of fullterm fetuses shows an essential difference among the individual cases only with regard to the lumen ratio (Table 5). On the other hand, each one is clearly distinguishable from aerated lungs. According to this study, the extension of the lumina does not have any significant influence on the finer structure of the lung in the human fetus, as long as the lung remains airless.

Conclusions can not be made on the basis of the cases reported above as to the fetal state of the lungs. As illustrated by table 11, they all show either signs of intra-uterine asphyxia or there was a complication during delivery which can be regarded to have caused premature respiratory movements and in this way, dilatation of the lungs. It is not at all evident that those lungs where the lumina were more extended should have been subjected to the influence of a factor producing stronger respiratory movements. Such knowledge as we have at our disposal does not allow of making any conclusions with certainty in regard to this question. It is further impossible, on the basis of these cases, to determine the size of the alveolar lumen at the moment of birth, before the inhalation of air in such cases where there were no factors disturbing the umbilical circulation. In one respect all these cases are similar: the

injurious factors directed against the baby during delivery were so strong that they caused death.

Live-born Infants. Aeration of the Lungs.

It is not possible to determine on the basis of my material how quickly the lungs become aerated in infants who are going to live and have a good respiration. Such infants as die in the course of the first few days after birth usually suffer from diseases or faulty development that have a restraining influence on the respiration and the rapidity of aeration of the lungs. One can therefore say that the results obtained from post mortem material represent in the first instance the slowest aeration.

My material is such that it is not possible to exclude from it cases where factors delaying the aeration are absent. However, I omit, to begin with, all those where factors greatly delaying the expansion of the lungs were to be found in the lungs themselves. I have therefore excluded all cases where formations of membranes could be ascertained. (See chapter concerning aspiration of the amniotic fluid). I am also omitting cases that showed an unmistakable disorder of the intra-thoracic development (Diaphragmatic hernia — cases N 967/II/45, N 534/II/45). The cases indisputably remaining also have a great number of factors influencing the respiration, but, as already said, it is impossible to obtain material that should not have any factors exercising influence on the respiration.

When determining the rapidity of the lungs' aeration with the aid of my material, I have been able to use as a basis of estimation nearly solely the circumstance, how soon the congenital atelectasis disappears (see animal experiments p. 40). When congenital atelectasis is used as a basis of determination it is imperative to draw a division between it and secondary atelectasis. It was possible to determine in the animal experiments the histologic difference between these two forms of atelectasis. In the post mortem material, there is a difficulty of finding a starting point, as it is hard to determine some area which has with certainty become atelectatic in a secondary manner.

As already mentioned in the survey of literature (p. 25), vernix membranes have been found only in aerated lungs, and it is consi-

dered that respiration is a necessary factor for their appearance. (My own researches point in the same direction). It can therefore be considered most probable that areas where these membranes are met with, have breathed. As these membranes are sometimes demonstrable also in atelectatic regions, the latter can be regarded as a type of a secondarily atelectatic area. The possibility cannot be denied that these can have partly collapsed first after death. In these cases also they represent aerated areas which have afterwards become airless.

Case N 494/II/45 had rather extensive atelectatic areas, where membranes could be found. (See Fig. 15) This baby had survived for 27 hours. Its condition after birth was good, according to the history of delivery. Microscopic examination of lungs revealed a great quantity of membranes in all sections. All the lobes showed atelectatic areas. The right lower lobe had the largest amount. When examining the atelectatic areas one could clearly dintinguish small lumina covered with membranes. The walls were tortuous. The shape of the lumina was irregular, both shape and size varying greatly. The walls were thick. The capillaries were rather full of blood, bulging somewhat into the lumen. The nuclei of their endothelial cells were oblong. It was difficult in some places to find alveolar epithelial cells. The form of the cells was low- or isoprismatic, but highprismatic cells were also found. There were 1—3 cells in one place — usually they were isolated. The plasma stained but slightly. The nucleus was round or oblong, sometimes angular or lengthened. Part of the nuclei was dark, without structure (pyknotic). The nuclei of the connective tissue cells were oblong, rather short, sometimes looking twisted. As a whole the tissue had an irregular appearance and seemed »in disorder», and it was sometimes difficult to distinguish among different kinds of cells.

These characteristics of secondary stelectasis conform rather closely to the picture which was obtained by means of animal experiments of lungs with secondary atelectasis, and correspond to the changes observed in aerated lungs. In order to draw the division between congenital and secondary atelectasis in each case one must try to establish, what are those essential and typical characteristics that divide these two forms of atelectasis from each other. The lumen size is no essential difference, as according to what has been

explained above, this size can greatly vary in lungs with congenital atelectasis. It seems however that the average variation is less in

TABLE 6

Characteristics of Congenital and Secondary Atelectasis in Lungs of Fullterm Infants

	Congenital atelectasis	*Secondary atelectasis*
Size of lumen	Small variations in same case	Wide variations in different places
Thickness of walls	Small variations. Generally thin	Wide variations. Often appear thick
Course and shape of wall	Tortuous course	Straighter course
Capillaries	Engorgement varies. Capillaries clearly distinguishable from walls, bulging out into lumina	Engorgement varies. Capillaries mainly on level of walls
Endothelial cells	Nuclei crescent-shaped or fusiform	Nuclei crescent-shaped
Alveoral epithelial cells	Clearly dinstinguishable from walls	Flush with walls
Form	Hight-, iso-, lowprismatic varying	High-, iso-, lowprismatic irregular
Nucleus	Round or elliptic, in centre or basally	Round, elliptic, angular generally in centre
Arrangement	1—3 in same place, of different shapes. Arrangement often irregular	1—3 in same place, of different shapes. Arrangement irregular
Mesenchymal cell nuclei	Fusiform, length exceeds thickness 2—4 times	Ditto
General aspect of lung	Regular, different places present same aspect. »Nice» structure	Irregular and varying appearance. »Coarser» structure

lungs with congenital than with secondary atelectasis. It also appears that the thickness of the walls varies less in congenital than in secondary atelectasis. Owing to these features, the structure of a lung with congenital atelectasis is more regular than in lungs affected with secondary atelectasis. Table 6 illustrates the characteristic features in different parts of a lung with congenital and secondary atelectasis. It is difficult to determine, to what an extent the characteristic features of secondary atelectasis described here can also be present in congenital atelectasis of a longer persistence. On the basis of animal experiments, it appears as if the areas must first become aerated before they are affected with secondary atelectasis.

When dealing here below with the rapidity of the inflation of the lungs, whose basis is the disappearance of congenital atelectasis, I did not consider myself justified in regarding as congenitally atelectatic other areas than such as have shown the characteristic features of it described above. It must be admitted that the basis of estimation is not quite free from possible errors. It is however practicable to check the results to a certain extent with the help of such cases that are free from atelectasis. Although the clinical knowledge is often incomplete, it still helps in the estimation of the cases. This being so, there are some possibilities to estimate the rapidity of the aeration of the lungs also on the basis of this material, duly considering the limitations described above.

The youngest case who showed strongly inflated lungs, died in the course of the delivery (Case K 719/45). The greatest part of the lungs was aerated. They were throughout of a mosaical light colour. Microscopical it was possible to ascertain that the basal parts of both lower lobes had unmistakably airless areas. The borders of these areas were very distinct (See Fig. 14). The airless areas were very few. The infant having died in the course of the delivery, this case proves that very extensive areas can become fully aerated as a result of only a few respiratory movements. It must be noted that the extended lumina were generally open »to the utmost» and the walls thin, threadlike. Although smaller lumina could also be found in several sections, they had unmistakably tense walls. Thus only the basal parts remained airless. Large areas of the dorsal parts were also aerated.

TABLE 7

Aeration of the Lungs in Fullterm Infants free from Membranes
Atelectatic Areas in Different Lobes

No and age.	*I*		*II*		*III*		*IV*		*V*	
	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa
N 458/I/45 18 min.	+	—	+	—	+	—	±	—	+	—
K 1823/45 3 ½ hours	+	—	+	—	±	—	+	—	+	—
K 2399/45 B 12 hours	±	—	±	—	++	—	+ ?	+ ?	—	++
N 2780/I/45 1 ½ days	±	—	±	—	++	—	±	—	±	—
N 1255/II/45 2 days	±	—	—	±	+	—	±	—	+	—
L 100/46 2 days	±	—	—	—	+	—	+	—	+	—
N 829/I/41 2 days	—	+	—	—	± ?	—	± ?	+	±	±
N 845/II/46 2 days	±	+	—	+	—	++	±	+	— ?	+
K 862/45 2 days	—	±	—	±	—	±	—	—	± ?	± ?
P 358/45 3 days	++	—	—	—	±	±	—	± ?	±	±
L 261/47 7 days	—	—	—	—	—	±	—	—	—	
L 272/47 7 days	—	—	—	—	—	±	—	—	—	±
P 363/45 11 days	—	—	—	—	—	±	—	—	—	±
L KP/45 11 days	—	—	—	—	—	±	—	—	—	—
L 122/45 1 month	—	±	—	—	—			—	—	±

Signs: — no atelectatic areas, ± small atelectatic areas, + middlesized atelectatic areas which do not comprise half of the area of specimen, ++ atelectatic areas being half or more of the area of specimen.

Ca = congenital atelectasis, Sa = secondary atelectasis, I = right upper lobe, II = right middle lobe, III = right lower lobe, IV = left upper lobe, V = left lower lobe

Table 7 illustrates the presence of congenital and secondary atelectasis in lungs free from membranes where respiration has occurred applying the above methods of determinaion. I have also paid attention to the contents. The precipitate appearing in congenitally atelectic lungs has no such definite character that it could not be regarded as due also to other reasons. A substance of a similar appearance is sometimes met whit also in lungs of older infants. Its absence gives however an indication to the effect that the area had become aircontaining, as this substance could be found in the lungs of all stillborn infants. No absolutely certain division between congenital and secondary atelectasis could be drawn in the areas of each one of the cases illustrated by the table. In the majority of cases however I find that the difference was sufficiently evident.

It can generally be seen in a lung that has breathed only for a short time and become only partly aerated, how only a part of the alveolar tree is expanded, and its peripheries retain flabby walls and small lumina. (Fig. 16, 17) This is regularly found in the lungs of infants who died in the course of the first three days of life. The same findings can be made in the lungs of those who died during delivery or were asphyxiated and did not resuscitate. The case K 719/45 (see above) is an exception, where the lumina were extended and the partitions thin in a throughout aerated area (See Fig. 14.) When the alveolar tree is only partly air-containing, its peripheral parts generally have morphologically the appearance of congenital atelectasis. This can therefore be considered to some extent as a normal phenomenon in the aeration of the lungs in cases where it takes place slowly. It is not possible to maintain on the basis of my material that this should always be the case — also if the aeration is rapid. To the contrary, case K 719/45 speaks against such a supposition.

When examining as a whole the clinical picture and the post mortem findings of the cases presented in table 7, we get an idea as to what an extent the aeration of the lungs can be regarded as possibly differing from corresponding »normal cases». (See table 12). It is to be noted then that nearly all were in a serious pathologic state, which can be considered as having exercised an influence on the character of the respiration. The six youngest infants had serious

asphyxia and several had had an impeded respiration the whole time. The seventh had a difficult respiration and the post mortem revealed a congenital heart disease, which must be considered to have made the continuation of life impossible. Congenitally atelectatic areas were found in all these cases. The youngest, of whom the delivery history does not say anything with regard to respiratory disturbances, were two days old (Cases N 829/I/41 and N 845/II/46). One of them revealed a cerebral hemorrhage, the other rupture of the liver and hemorrhage into the abdominal cavity. Both cases show small areas of congenital atelectasis. Case N 845/II/46 can be taken to have breathed well at first, and to have therefore approached the »normal». These cases have larger areas affected with secondary than with congenital atelectasis. Case K 862/45 is normal in so far, as nothing pathological was observed during the first day of life, and the baby died unexpectedly and suddenly. The lungs did not show at all any unmistakable areas with congenital atelectasis. The left lower lobe had small atelectatic areas of which it was impossible to say whether they were congenital or secondary. In an infant aged three days who was sleepy and slow to react (case P 358/45) and in whom the post mortem revealed a cerebral hemorrhage, areas were found in the lungs that could be regarded with certainty as congenital atelectatic. Only in the lungs of an infant a week old was it possible to establish a total absence of congenital atelectasis (L 261/47). This baby died suddenly.

As illustrated by the table, the lungs are aerated everywhere only as late as in infants about two days old — up to that time extensive atelectatic areas are to be found at least in one lobe (marked on the table + or ++), and not only a few areas or a penetration of air into some part of the alveolar tree only (marked on the table ±).

Although the microscopic examination revealed that the lung was air-containing everywhere, and there were even no sections of the alveolar tree unmistakably airless, the walls seemed to be of a different thickness. Case K 719/45 had thin threadlike walls, but in case K 862/45, which was aerated throughout, the walls were quite clearly thicker. In a baby who had lived 7 days the walls were again unmistakably thinner — and this was also the case in

an older infant. It can therefore be said that the aeration of all sections and consequently the absence of atelectasis does not prove that the lung is fully expanded, but also such cases who have these characteristics show an aeration of different degrees. This circumstance makes a comparison of the aeration in different cases more complicated than can be supposed solely on the basis of a macroscopic examination. — It must be admitted of course that post mortal changes can partly cause differences, therefore one must be careful when making conclusions on the basis of these findings.

Conclusions. — The lungs can become almost completely aerated alreadey after a few inspirations.

The lungs in my post mortem material were unmistakably aerated everywhere in infants 7 days old. However, already such infants who had died aged 2—3 days, can have lungs nearly free from congenitally atelectatic areas. In such cases there have generally been factors which weakened the condition of the baby. Atelectatic areas persisted for the longest period of time in the lower lobes. Secondary atelectasis can already be found in infants one day old. Cases who do not have atelectatic areas, are exceptions in the post mortem material.

The aeration of the lungs where membranes could be found will be taken up in connection with the aspiration of amniotic fluid.

Premature Infants

Stillborn and Asphyxiated who Did not Resuscitate. Congenital Atelectasis.

There are only five *stillborn infants* in my material weighing < 2500 gm, the weight varying from 670 to 2000 gm. One of them died during pregnancy (Case K 591/45). The weight at birth was 1930 gm. The fetus was somewhat macerated. The inner organs were soft. The lungs were macroscopically airless. Microscopically all sections presented a similar picture. Lumina were demonstrable in the alveoli. Their epithelial cells had for the most come off. The shape of the cells adhering to the walls was high- or isoprismatic. The erythrocytes were clearly visible in the

capillaries and judging by them there was a great number of capillaries.

The smallest of those who had died during delivery were the twins K 425/45 A and B. — The weight of the B-fetus at birth was 670 gm. Macroscopically the lungs were airless -- the surface did not show anywhere aerated areas, but had the same appearance throughout, of a greyish-red colour. Microscopically it was possible to determine that the lumina of the anterior part of the right central lobe were unmistakably more extended than elsewhere. There were no significant variations otherwise, either when measuring by the eye or counting the lumen ratio (see table 8). In the areas with small lumina (8—10 %) the cells lining them were high or isoprismatic. (Fig. 18. See also Fig. 23) They were lining the main part of the lumen but here and there loops of capillaries could be seen among them in direct contact with the lumen. Protoplasma in the cells stained either feebly or not at all. The nuclei were oblong or round, lying in the centre of the cell or somewhat eccentrically, when they where often farther away from the base than from the surface. The diameter of the nuclei was about half of the diameter of the cells. The alterations of the forms of the cells were usually insignificant, — yet there were sometimes cells strongly differing in shape from the others in the lining of the same lumen (highprismatic, isoprismatic). The arrangement of the cells was often regular, but sometimes not — there were places where the lumen was insignificant — and it could then be noted that they had formed epithelial layers. The abundance of capillaries varied in different places and it was often possible to find capillaries only in the basal parts of the epithelial layer; their coils did not in that case penetrate among the epithelial cells. The extension of the capillary coils which reached the lumen varied from areas of the width of one epithelial cell to areas corresponding to the width of 3—4 such cells. The nuclei of the capillary endothelial cells were clearly visible. The extreme periphery (pneumonomeres) were most deficient in capillaries, and the greatest capillary coils lay in the somewhat more central parts. The lumina were generally empty. The whole had an appearance of regularity and the lumina were clearly distinguishable by reason of their light epithelium. The tissue between the cavities was loose,

its cells had oblong or fusiform nuclei. It was not clearly distinguishable by staining from the epithelium, the only difference being that the protoplasma in the cells took on a somewhat stronger staining. Nothing was seen there that resembled a staining proper to connective tissue. Only around the blood vessels there were collagenic and elastic fibres. The sections had some places where cells with the exact appearance of epithelial cells formed an islet devoid of lumina within the tissue, that was clearly bounded by the surrounding loose tissue. There were also similar islets formed by a few cells and also places where the lumen was quite insignificant. I have regarded these forms as being caused by a dissection of different places.

The weight at birth of twin A was 850 gm. In the anterior part of the lungs it was possible to distinguish very few light-coloured aearated areas, differing from the rest of the tissue. Microscopically the structure of the lungs was not different to that of the B-fetus.

Case N 352/II/45 (weight at birth 1040 gm) did not reveal macroscopically any areas differing from the rest of the structure. Microscopically there was a small area in the right lower lobe with extended lumina. (Fig. 19 — see also Fig. 28.) Elsewhere they were small but distinct. The structure differed clearly from the preceding. The cells lining the lumen were of the same form as above, but they did not line the lumen nearly as uninterruptedly, there being usually 2—5 cells close to each other and coils of capillaries in the spaces between. The capillaries were unmistakably more abundant than in the cases K 425/45 A and B. The walls were thinner — they appeared now as partitions and the aspect was not at all similar to the above where the epithelial part was seen as some kind of an islet in the loose mesenchymal tissue. The tissue in the walls was not different to what has already been described.

Case N 1521/II/45 (weight at birth 2000 gm.) showed macroscopically an area in the front part of the right central lobe that was clearly different from the rest, as it was of a light colour and air-containing. A microscopic examination revealed here extended lumina, but the size of the lumina varied greatly. (Fig. 20) There were also extended lumina in the left upper lobe, but a very small number of areas without any lumina could also be noted. The tissue structure greatly resembled the lungs of fullterm fetuses —

yet there were unmistakably more alveolar epithelial cells and less capillaries than in the fullterm. The cells had an iso- or highprismatic form.

TABLE 8

Prematures who Died During the Labour
Lumen ratio

Number	Birth weight	Lumen ratio (%)					Remarks
		I	II	III	IV	V	
K 425/45 A	850 gm	18	12	13	10	12	Aeration
K 425/45 B	670 gm	11	19—13	9	10	8	,,
N 352/II/45	1040 gm	7	5	6	—	—	Area in III where lumen ratio 34 %
N 1521/II/45	2000 gm	25	80	15	3	—	In II part as in III and part is extended, where lumen ratio counted

Signs: I = right upper lobe, II = right middle lobe, III = right lower lobe, IV = left upper lobe, V = left lower lobe.

Table 8 illustrates the lumen ratio in the lungs of prematures who died during delivery. Even if it is not possible to make any conclusions on this basis as to the extension of the lumina in the fetal state, any better than with regard to the fullterm fetus, it can yet be maintained that lumina are to be found everywhere in the lungs of stillborn premature infants. As already mentioned in the survey of literature, there are according to BENDER's researches unmistakable lumina in the pneumonomeres during the whole evolution-process of the lungs. The method of calculation described above yields different results regarding the relative size of the lumen in the fullterm and the premature infant — especially for the smaller premature — owing to the circumstance that when counting as described, the extensive tissue area between the pneumonomeres proportionally reduces the lumen ratio. Taking this into consideration, it can still be maintained that the lumina look smaller in the premature than in the fullterm baby. The microscopic structure of congenitally atelectatic lungs of the premature is different in different cases, depending on the stage of development of the fetus. In the

fetus who had the lightest weight in my material the cells lining the lumen were mainly high prismatic. With the increase of the weight at birth it appears that the relative proportion of the cells decreases and at the same time the number of capillaries reaching the lumen grows. A regular structure of the tissue is characteristic of congenital atelectasis.

Live-Born Premature Infants. Aeration of the Lungs.

The preceding reports show that the difference in structure of the lungs of premature infants depending on their weight at birth is so significant that it appears advi able to make a special study of the aeration in different weight groups. Accordingly, I have divided my material into two groups *Immaturus* (weight at birth < 1250 gm) and *Praematurus* (weight at birth 1250—2499 gm).

Immature Infants. — There are twelve cases in all. Only four of them are such where no membranes were demonstrable. They all died in the course of the first 24 hours. Table 9 presents their weight at birth, age and aeration of the lungs. The difference is most pronounced between the two who had lived longest (N 210/II/45, L 26/46) and is evidently greater than what could be expected as due solely to the difference in the term of life. In both cases a subdural hermorrhage was found, which was regarded as the cause of death. The sections of lungs show an unmistakably different structure — especially in the abundance of capillaries. The baby with the greater weight at birth showed a larger number of capillaries attaining the lumen than other one with the lesser weight. No difference was evident regarding the form of the cells, because case N 210/II/45 had post mortal changes hampering the estimation. The pulmonary structure of the three with the lightest weight at birth showed but little difference, both with regard to the structure itself and to the expansion of the lungs. The aeration was insignificant everywhere and limited to the central part of the alveolar tree that was not fully developd. The structure of the parts with small lumina was the same as described above in case N 352/II/45. There are variations in the number of capillaries, but not sufficient to be demonstrable when measured by the eye.

TABLE 9

Aeration of the Lungs in Immature Infants free from Membranes

Number	*Birt weight*	*Age*	*Aeration*
N 446/I/45	1020 gm	1 hour	Peripheral parts of »arbor alveolalaris» not expanded, their lumina small. »Bronchioli» and »alveolar ducts» have tense arched walls in places. In right middle lobe »alveolar» lumen also somewhat expanded.
N 852/I/45	980 gm	2 h. 15 min.	Rather similar to the above.
L 26/46	970 gm	19 hours	Clearly extended lumina — in main part of right middle lobe up to periphery, similary in some places of upper lobe. Otherwise as above.
N 210/II/45	1240 gm	23 hours	In all lobes expanded areas reaching periphery — estimated at half the area of section, in right middle lobe more than half.

The material comprises a case with a weight at birth of 970 gm, who had lived for 5 days (P 203/45), and had a scant number of membranes. *) A structure unmistakably different to what has been described above in connection with congenitally atelectatic lungs, was found in the left lower lobe with a half-collapsed lumen lined by membranes. (Fig. 21) The cells had an irregular form, vaguely fusiform, and appeared to be flush with the wall. The cells did not appear in regular formations, but one or two together, and the variations in shape among them were considerable. The cell nucleus was oblong or angular (often dark, pyknotic). The total number of cells seemed to be much less than in a stillborn immature infant of the same weight. On the other hand, the number of capillaries

*) The specimen taken from the right upper lobe of this case showed inflammatory changes in a restricted area, mainly however in the »bronchioli».

appeared greater. The difference from congenital atelectasis was very much pronounced. There was every indication that these areas were affected with secondary atelectasis. Their tissue structure can be considered as characteristic of secondary atelectasis. It is to be noted especially that also the shape of the cells in this case is clearly different to that of the lung with congenital atelectasis. (Compare with results of observetions on lungs of the fullterm infants). This variation in the cell shapes conforms to FARBER's observations.

With a view to studying these differences of structure, I have deemed it advisable to examine other immatures in whom membranes were found. In addition to those described above, there were seven such cases in all. In case N 935/I/45 (weight at birth 1090 gm and age 6 ½ h.) two kinds of lumen, regular and irregular, were clearly distinguishable. In the irregular lumina the cell form was also irregular, isoprismatic or lower. The cells had the appearance of being plastered along the walls and took on sometimes a fusiform shape. The contours of the lumina were irregular here — the walls tortuous. There were often membranes in the irregular lumina, but they were absent in regular ones. There were also some irregular without membranes. The supposition seems justified that those with an irregular shape are areas affected with secondary atelectasis In other subjects placed into the immature group because of their weight an irregularity of the shape of the lumen was found in such areas which were probably secondarily atelectatic. Alterations in the form of the cells were much rarer and difficult to determine. It is noteworthy that the majority of the cases died during the first 24 hours, which tends to show perhaps that such changes need a longer time. When estimating the character of atelectatic areas in the lungs of immatures who survived for a short time, it can therefore be said that it is clearly more advisable also in these cases to study the irregularity of the lumen rather than of the cell forms in order to differentiate between congenital and secondary atelectasis, although the shape of the cells can also be of use in the estimation.

As illustrated by table 9, the expansion of the lungs of the immatures often had the same character as in the fullterm lung — i.e. only part of the alveolar tree had become aerated, while the peripheries retained their congenitally atelectatic structure. Yet in immatures less than 1000 gm weight and under a day old, lumina

could already be found that were extended up to the extreme periphery (case L/26/46). Case K 720/45 (weight at birth 920 gm, age 1 ½ h) proves that some part of the immature lung can become fully aerated within a short time. This subject had but a small number of membranes. In a specimen taken from the right central lobe all the lumina were expanded to the utmost. (Fig. 22) This expanded area showed in some places isoprismatic cells up to 8 one after another, and the cell form was isoprismatic, the cells being similar to each other as to shape and clearly distinguishable from the other parts of the walls. In the whole material there was only one immature in whose lungs no congenitally atelectatic areas could be found (P 203/45). — This case died 5 days old.

In case P 203/45 it seems that the number of capillaries extending up to the lumina was considerably greater than in other immature babies of the same weight who had died in the course of the first 24 hours. In the other cases it was not possible to find more capillaries extending into the lumen, in the aerated than in the congenitally atelectatic areas, and it does not therefore seem justified to draw any definite conclusions on the basis of the case in question. The ability to distinguish capillaries in sections of this kind greatly depends on their engorgement, which hinders the comparison between different cases and renders it uncertain.

With regard to *areation of the lungs of immature infants*, the following can be maintained on the basis of this material: The lungs did not become fully aerated everywhere in the course of the first 24 hours. Some part of the lung can then be air-containing in such a way, that the lumina are open up to the extreme periphery — already in babies under two hours old. Lungs of infants who died five days old can be free from congenitally atelectatic areas.

Premature Infants. — My material comprised 11 premature infants free from membranes and under two weeks of age (not counting the immatures). One of them had diaphragmatic hernia. (K 970/41). The weights at birth of these infants varied between 1270 and 2430 gm and their age was from 13 minutes to 9 days.

The differentiation between congenital and secondary atelectasis in the premature is possible along the same lines as described above

where fullterm and immature babies were concerned. Although the lungs are different as to structure from the lungs of fullterm infants, the premature are nearer the fullterm than the immature with regard to structure of the epithelial cells and the umber of capillaries. This is naturally most evident in those whose weight at birth approaches 2500 gm, ut even close to the nether limit the structure greatly resembles that of fullterm babies. The difference lies in the circumstance that, when measured by the eye, the premature have less capillaries and more epithelial cells than the fullterm. Yet the borderline is by no means pronounced, and therefore it is possible to meet with cases in this group approaching the nether limit, where the pulmonary structure greatly resembles that of the immature (case N 788/I/45 — weight at birth 1360 gm.). (Fig. 23) Such aspects can also be seen in infants with a considerably greater weight at birth (K 2621/45 — weight at birth 2080 gm.). (Fig. 24) There is however a difference in the forms of the cells lining the walls, especially when compared to those weighing under 1000 gm, as the majority of the cells in the premature are unmistakably lower — they are isoprismatic, whereas the cells of the immature are mainly high prismatic.

The quantity of capillaries reaching up to the surface of the lumina is some kind of a criterion of the development of the lungs. It is however evident that when examining the number of capillaries in an ordinary section, only such capillaries where there is blood, are seen and taken into consideration. Capillaries empty of blood, on the other hand, are so difficult to find, that it is impossible to make any comparisons of the quantity of capillaries on the basis of such studies. It appears evident that there are individual variations in the quantity of capillaries, nor does their quantity solely conform to the variations of the weight at birth.

In order to draw the division between congenital and secondary atelectasis I have made use, in the first place, of the differences in the shape of the lumen and in the position of the epithelial cells on the walls. I have also paid attention to the form of the cells, and it seems as if these also underwent sometimes variations similar to those described above in case P 203/45. I feel this has been the case with subjects whose weight at birth was under 1250 gm or thereabout. In case P 76/45 (weight at birth 1300 gm — age 9

days) the cell form was low, irregular, but there were also to be found isoprismatic cells of a regular shape in lumina of an irregular form and where the position of the cells on the walls was the same as in lumina with secondary atelectasis.

Although the pulmonary structure is different in different cases of premature infants, and the differentiation between congenital and secondary atelectasis sometimes difficult, I have endeavoured to illustrate by table 10 the aeration in the lungs of my cases free from membranes. According to this, the lungs of these cases did not expand fully in the course of the first three days, congenitally atelectatic areas being noticeable in one or several lobes. As already mentioned, there are cases where it is difficult to determine whether some area is affected with congenital or with secondary atelectasis. This is e.g. the case with subject K 1019/45. Here lumina could be seen that had a regular form, and the form and arrangement of the cells where exactly as in congenitally atelectatic lumina. But there were others of a regular shape, with 3 to 4 isoprismatic cells close to each other rising from the walls in regular formations, and a lumen with every appearance of secondary atelectasis could be seen in the close vicinity. In such cases I did not feel I had any certainty as to whether the said area was to be considered congenitally or secondarily atelectatic. The examination of extended lumina after breathing has revealed that even when the lumen unmistakably expands, some cells can retain their shape and the position on the walls characteristic of lungs with congenital atelectasis. — In cases where such questionable cells were in evidence, it was however often possible to find areas which were undoubtedly to be regarded as congenitally atelectatic, therefore this circumstance is of no particular significance where a general estimation is concerned.

When studying the post mortem findings and clinical observations on the prematures, such pathologic states can be found very often, which may be thought to have influenced the respiration. A considerable part had intracranial hemorrhages and mention was often made in the reports of a respiration impeded in some way. (See table 14).

It is therefore evident that post mortem material reveals a most slow aeration, and it is quite possible that it takes place much more

TABLE 10

Aeration of Lungs in Premature Infants free from Membranes

No birth-weight and age	I		II		III		IV		V		Remarks
	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	
N 788/I/45 1360 gm 13 min.	++	—	++	—	++	—	++	—	++	—	
K 2621/45 2080 gm 30 min.	++	—	++	—	++	—	++	—	++	—	
N 717/I/45 2150 gm 9 ½ hours	±	—	—	±	±	±	±	±	±	±	
K 1919/45 A 2430 gm 22 hours	±	±	± ?	± ?	+	—	± ?	± ?	+	—	
N 1043/I/41 1750 gm 18 ½ hours	±	—	—	—	±	±	±	—	—	+	
L 129/47 2000 gm 2 days	—	±	—	±	—	+	±	+	±	+	Lumina full of blood, extendet, but structure blurred by blood
P 370/45 1270 gm 3 days											
P 172/45 1300 gm 4 days	—	—	—	—	—	±	—	—	—	±	
N 463/II/45 2180 gm 6 days	±	±	—	—	±	±	±	±	—	± ?	
L 108/47 1620 gm 7 days	—	++	—	++	—	++	—	+	—	+	
P 76/45 1300 gm 9 days	—	±	—	—	— ?	±	±	±	—	±	

Signs: — no atelectatic areas, ± small atelectatic areas, + middlesized atelectatic areas which do not comprise half of the area of specimen, ++ atelectatic areas being half or more of the area of specimen.

I = congenital atelectasis, Sa = secondary atelectasis. I = right upper lobe, II = right middlelobe, III = rightlowerlobe, IV = leftupperlobe, V = leftlower lobe

rapidly in healthy undamaged prematures with unimpeded respiration, than in those who have been the object of this study.

Conclusions

The lumen of unaerated areas in the lungs of stillborn premature infants is small, but its presence can be established in any case. The lumina are smaller than in the fullterm babies, but the material does not justify conclusions as to the growth of the lumen according to an increase in weight. Estimation is rendered more difficult by the circumstance, that the lumina may be extended in consecquence of premature respiratory movements due to the effects of labour.

In aerated lungs no distinct difference can be ascertained in the mode of expansion. Both in fullterm and premature babies the lumen may often expand in such a way, that only a part of the alveolar tree in the process of development expands, whereas a part remains congenitally atelectatic. Yet all the lumina can be extended »to the utmost» in some part of the lungs of immatures under 1000 gm weight at birth. Such an extension can also be seen in small areas in babies who died during the delivery. In consequence of differences in the pulmonary structure it is not possible, where the prematures — and also the immatures are concerned, to establish a histologic difference common for all between congenital and secondary atelectasis, as this is possible with regard to fullterm babies. The difference lies in the alterations in the shape of the lumina and of the cells in their walls.

My post mortem material speaks on behalf of a gradual aeration in the lungs of prematures, so that lungs that are or have been fully aerated can only be found in babies who had survived for 4 to 5 days. It is evident that on the basis of this material no conclusions can be drawn as to how quickly the aeration takes place in healthy undamaged prematures. However, the material speaks for the supposition that the aeration is gradual also in these latter, as congenitally atelectatic areas were revealed by autopsy in infants three days old also in such cases, where nothing special could be found in the state of the baby after its birth.

The aeration is perhaps somewhat slower in premature than in fullterm infants, but according to this material, the »utmost» rapidity is not so very different for both these groups.

2. On Amniotic Fluid Substances in the Lungs

The cases are divided into two groups, with or without membranes in the lungs. I have however deemed it advisable to deal partly in both groups with stillborn and asphyxiated infants who did not resuscitate.

It is easier to determine and in different cases to compare the amount of aspirated substances in the group free from membranes than in the other. Even in such cases the comparison is rendered more difficult by the circumstance that the amounts cannot be compared to each other numerically. The counting of the squameous epithelial cells of the amniotic fluid in the lumina would hardly be of any use, because it is to be supposed that their number in the amniotic fluid varies in individual cases. This holds evidently good also with regard to drops of fat. The precipitate constantly found in the lungs of the stillborn probably has its origin in the liquor amnii — at least partly. It is very difficult to determine the amount of this material. It must be taken into consideration that with the preparation of the section, some substances may have become detached from the lumen, and their amount can be different in different cases. I have not endeavoured to make any exact estimation, but have contented myself with very summary estimations of the amounts of different substances in the lumina. I have marked the amounts of these substances on the tables as ± (small), + (medium) and + + (abundant). I have endeavoured to apply the same scale in different cases, as much as this was feasible when measuring by the eye. I have not paid any attention to the quantities of lanugo hairs and meconium in the lungs, as these make the estimation of the extent of the aspiration even more difficult than by means of the above principles.

Cases free from Membranes

I shall deal at first with fullterm and premature infants as two different groups.

Fullterm infants

Epithelial cells and squamae from the amniotic fluid were to be found without exception in the lungs of *infants who died during pregnancy or at birth, and of the asphyxiated who did not resuscitate.* Table 11 illustrates the quantities of the substances found estimated according to the abovementioned method. If the amount of particles (i.e. epithelial cells and squamae of the amniotic fluid) in the lumina is taken as a basis, strong aspiration had occurred in 5 cases who died during delivery. Compression of the cord was found in three of them. In two others the amniotic fluid was discoloured, and in one of them a deterioration of the fetal cardiac sounds could be established during labour. The strong aspiration in these cases can therefore be considered as due to intrauterine asphyxia. On the other hand, there were five who died during pregnancy or at birth, where compression of the cord was present, but a medium (three cases) or small (two cases) quantity of patches was found. In three other cases who died during delivery there was a medium quantity of patches. In two of them observations were made which may be taken as an explanation of the aspiration that had occurred (cases N 965/II/41 and K 3189/45). One case had an insignificant amount of substances (N 847/II/41) and nothing special was said about the delivery, but that it had lasted for a long time. This case can be regarded as representing the »physiological» aspiration. It must be admitted, that this case diverges so much from an ordinary delivery, that the aspirated amount need not be such where labour has proceded without disturbances.

In addition to the forementioned particles, fat drops were a constant finding. Their quantity was generally about similar to that of the liquor amnii epithelial squamae and cells. There were some exceptions. As the fat substance in the amniotic fluid can vary in individual cases, it is easy to understand that the amount of aspirated fat drops also can vary due to this reason. When staining frozen sections, e.g. transferring them from one staining solution to another, one runs a greater danger of the substances dripping away than when staining paraffin sections, in which case the specimen is fixed on glass. I therefore feel that the idea gained from paraffin sections is nearer the truth than that given by staining fat. I have

TABLE 11

Aspiration of Amniotic Fluid in Fullterm Stillborn and Asphyxiated Infants who Did not Resucitate

Number	Aspiration quantity	Intra-uterine asphyxia	Complications of labour Post mortem findings
N 626/II/45	Particles +	Discoloration of amniotic fluid	Umbilical cord squeezed in hand of fetus. Ecchymoses
	Other subst. ++		
	Fat +		
N 2659/II/45	Particles +	Cardiac sounds ceased, no other observations	Ecchymoses
	Other subst. ++		
N 1634/I/45	Particles ++	Strong discoloration of amniotic fluid	Ecchymoses
	Other subst. +		
	Fat ++		
N 810/II/45	Particles ++	Discoloration of amniotic fluid. Cardiac sounds weakened gradually	Ecchymoses
	Other subst. ±		
	Fat ++		
N 847/II/41	Particles ±	Amniotic fluid ordinary	Prolonged labour Leptomeningeal edema
	Other subst. ++		
	Fat +		
N 965/II/41	Particles +	Discoloration of amniotic fluid	Pelvic presentation Congenital hydrocephalus
	Other subst. +		
	Fat +		
N2246/II/45	Particles +	—	Strangulation by the cord. Congenital hydronephrosis
	Other subst. ++		
	Fat +		
N 2686/II/45	Particles +	Amniotic fluid ordinary. Cardiac sounds weakening then ceasing	Prolapse of the cord
	Other subst. ++		
	Fat +		
K 719/45	Particles ++	Amniotic fluid somewhat discoloured	Strangulation by the cord. Subdural hemorrhage
	Other subst. +		
	Fat ++		
N 2143/I/44	Particles ±	—	Prolapse of the cord
	Other subst. ++		
	Fat +		
K 643/46	Particles ++	Amniotic fluid somewhat discoloured	Strangulation by the cord. Adrenal hemorrhage
	Other subst. +		
	Fat +		
N 906/I/46	Particles ++	No cardiac sounds to be heard	Prolapse of the cord
	Other subst. ++		
	Fat +		

Number	Aspiration quantity	Intra-uterine asphyxia	Complications of labour Post mortem findings
K 3189/45	Particles +	Cardiac sounds	Abruption of the placenta. Acute anemia of the fetus
	Other subst. +	ceased	
	Fat +		
K 1811/45	Particles ±	—	Prolapse of the cord. Congenital microcephalus. Ecchymoses
	Other subst. +		
	Fat +		
N 979/I/46	Particles ±	—	Pelvic presentation Ecchymoses
	Other subst. +		
	Fat ±		
N 676/II/46	Particles +	—	Rupture of the liver
	Other subst. + +		
	Fat + +		
K 1114/45	Particles +	Discoloration of amniotic fluid	Fetal hydrops.
	Other subst. +		
	Fat +		
N 2089/II/45	Particles ±	—	Face presentation. Subdural hemorrhage
	Other subst. + +		
	Fat + +		

made no attempt to classify on the tables substances which did not possess any definite form, instead of which I have used the general heading »other substances». The majority of them were seen as a precipitate; when stained with WEIGERT's hematoxylin and VAN GIESON they took on a yellow or yellowish-grey colour, DELAFIELD's hematoxylin and eosin produced rose, and MASSON — a purple staining. The elements did not as a rule take on mucicarmine, although bronchial glandular cells of the same section were stained an intense and clear red colour, — they can have had some fibre or particle staining red. In some cases the substance fully resembled the serum to be found in blood vessels, both with regard to staining and form. It is probable that this substance is mainly amniotic fluid, but one cannot with certainty distinguish it from edema fluid, although this latter is generally of a more homogeneous nature. It evidently depends on the protein contents of this substance, as to what an extent it becomes visible, which makes it clear that this amount also varies more in individual cases, than what whould be compatible with the aspiration occured.

There is one case in the group of asphyxiated who did not resuscitate (K 1114/45), who may have died from causes that had nothing to do with the delivery (Fetal hydrops). It was also noted in this case in the course of the delivery that the amniotic fluid was discoloured and therefore the moderate aspiration observed should still perhaps be considered greater than in a normal delivery. In the other three cases no mention is made of intra-uterine asphyxia. They had a small or medium amount of patches. The circumstance that these babies evidently died in consequence of the process of delivery makes it probable that factors influencing the aspiration have also been at work here.

It is therefore possible to say that one cannot, by examining the lungs of babies who died during pregnancy or delivery and of asphyxiated who did not resuscitate, get an idea of the amount of substances present in the lungs at the beginning of labour, not even of the state of things as they are when a normal delivery has come to an end. Only if the fetus had died without having had any possibility to aspirate, would it be possible to draw conclusions as to the »normal» amount of aspiration.

It is difficult to determine to what an extent the aspiration alone can be regarded as the cause of death of infants who died during pregnancy or delivery, or of asphyxiated who did not resuscitate. In order to consider the baby to have been suffocated by the amniotic fluid, it must be insisted upon that the autopsy should reveal signs of attempted respiration. Not a single case did show in the trachea or bronchi any such abundant amounts of aspirated substances, that they would justify a supposition of having fully obstructed a deeper penetration of the air. This being so, air must be found in the lungs as a mark of respiration, before it is possible to ascribe the suffocation to the liquor amnii. Otherwise the aspiration must be so strong that the amniotic fluid substances should entirely fill the lumina. Yet it is demonstrable that even in cases of a strong aspiration, the liquor amnii substances only fill part of the lumina (e.g. case K 643/46), part of them being air-containing. (Fig. 25) Moreover, in addition to a strong aspiration, the lungs have sometimes become aerated to a considerable degree, but the fetus had died nevertheless in the course of the delivery. (Case K 719/45). Although aspiration can have a share in the cause of death in these

cases, the possibility must be taken into consideration that the deficiency in oxygen suffered by the fetus in consequence of compression of the cord, was an important factor, more important perhaps than the aspirated amniotic fluid.

Live-Born Fullterm Infants. — Particles of the amniotic fluid sunstances could be found in the lungs of all the live-born infants under 4 days old. (Table 12). The amounts were not especially abundant in any of these cases. Of the four who died in the course of the first 24 hours two had a medium and two small quantity of these particles. Only one of them was such as could be considered to have died of causes unconnected with the delivery (N 967/I/41). The autopsy revealed as cause of death a rightsided diaphragmatic hernia — the right lung was small — only about a quarter of the left. There was a small number of particles of the amniotic fluid and a medium quantity of fat and other (indeterminable) material. This case is the one of all four that most approaches the »normal» with regard to changes caused by the process of delivery. As there were malformations in the thoracic cavity which had an evidently impeding influence on the breathing, it can be supposed that the aspirated amount was next to the minimum quantity. In the other three cases there were factors that can be regarded as having caused the aspiration, and therefore they do not give any idea as to the amount of aspiration in a live-born »normal» infant.

It is to be taken into consideration already for infants who lived but a short time, but still more for those who survived for several days, that the amount of material to be found in the lungs is by no means the same as at the moment of birth. It is of course evident that the discharge of foreign substances from the lungs begins immediately after the onset of respiration. Even if the lungs retain some quantities of these substances, they cannot be considered to be equal to the amount at the moment of birth, nor is it possible to draw any conclusion on the basis of the remaining quantities, how much substance there was in each case at the moment of birth. Particles of the amniotic fluid were not to be found in my material in infants more than ten days old, and in one case (L 100/46) there were but isolated patches of epithelial cells and squamae from the skin of the fetus in an infant only two days old. No amniotic fluid

TABLE 12
Aspiration of Amniotic Fluid in Fullterm Infants under 4 Days old
(Cases free from Membranes)

Number, age	Aspirated quantity	Symptoms of asphyxia	Complications of labour Post mortem findings
N 458/I/45	Particles +	Discloration of amniotic fluid. Born asphyxiated	Pelvic presentation
18 min.	Other subst. +		Ecchymoses
	Fat +		
N 967/II/41	Particles ±	—	Diaphragmatic
50 min.	Other subst. +		hernia
	Fat +		
K 1823/45	Particles ±	Discoloration of amniotic fluid. Born asphyxiated	Subdural hemorrhage
3 ½ h.	Other subst. +		
	Fat ±		
K 2399/45	Particles +	Born strongly asphyxiated	Transverse presentation. Subdural hemorrhage
12 h.	Other subst. +		
	Fat ±		
N 2780/I/45	Particles ±	Fetal asphyxia	Prolonged labour.
1 ½ days	Other subst. +	Born asphyxiated	Fracture of frontal
	Fat + +		bone. Subdural hemorrhage
N 1255/II/45	Particles ±	Born strongly asphyxiated	Congenital atresia
2 days	Other subst. +		of the duodenum
	Fat +		Diffuse peritonitis
L 100/46	Particles ±		Congenital heart
2 days	Other subst. ±		disease
	Fat ±		
N 829/I/41	Particles +	—	Leptomeningeal
2 days	Other subst. +		hemorrhages
	Fat + +		
N 845/II/46	Particles ±	Amniotic fluid grey?	Rupture of the liver
2 days	Other subst. +		
	Fat +		
K 862/45	Particles +	- -	Mors subita
2 ½ days	Other subst. +		
	Fat		
P 358/45	Particles ± ?	?	Intraventricular hemorrhage of the brain
3 days	Other subst. +		
	Fat +		

substances were found in the lungs of a seven days old baby (N 272/47), but another of the same age showed particles which reminded of the squamae found in the amniotic fluid (L 261/47).

Premature Infants

As there does not seem to be any considerable difference in the amounts of amniotic fluid aspirated by immatures and prematures, I have not considered it necessary to put them into different groups in this connection.

TABLE 13

Aspiration of Amniotic Fluid in Stillborn Premature Infants.

Number and birthweight	Aspirated quantity	Symptoms of asphyxia	Complications of labour Post mortem findings
K 591/45	Particles +	—	Died during pregnan-
1930 gm	Other subst. +		cy. Congenital heart
	Fat ++		disease
N 352/II/45	Particles ++	—	Died during labour
1040 gm	Other subst. +		Ecchymoses
K 425/45 A	Particles ±	—	Hydramnion.
850 gm	Other subst. ±		Died during labour
	Fat ±		
K 425/45 B	Particles +	—	Hydramnion
670 gm	Other subst. ±		Died during labour
	Fat ±		Ecchymoses
N 1521/II/45	Particles +	—	Eclampsism of preg-
2000 gm	Other subst. ±		nancy. Died during
	Fat +		labour. Leptomenin-
			geal hemorrhages
N 1027/II/41	Particles — ?	—	Strongly asphyxia-
2220 gm	Other subst. ±		ted, not resuscitated
	Fat ±		

Table 13: The only fetus who had *died during pregnancy* had a medium quantity of liquor amnii particles. The cause of death was not revealed, as although Cor tricolulare was found at the post mortem it cannot of course be considered as the cause of death without any further question. Even if the cessation of the heart function is regarded as the cause of death, it must be still taken into consideration that respiratory movements could be made in that case at the moment of death. The delivery histories never made any mention of symptoms of intrauterine asphyxia in these cases. As the post mortem revealed positive findings in but

one case, and then only piarachnoid hemorrhages which are hardly adequate as a cause of death, -- it seems advisable to consider as such in the first place trauma at the time of delivery, to which the delicate premature organism has succumbed. -- Abundant aspiration was ascertained in one case only (N 352/II/45). Here the aspiration was so strong that the fetus might be considered to have been suffocated by the amniotic fluid, as the lungs showed that attempts at respiration had been made -- some clearly extended lumina. The smallest amount of aspiration was found in the largest fetus of the whole group. Some patches could be seen, which must probably be interpreted as squamae. The lungs were partly air-containing and they were affected with interstitial emphysema. Perhaps part of the substances in the lungs of this case may have disappeared but it is difficult to believe that great amounts should have disappeared in so short a time, if they had been originally abundant.

In the lungs of stillborn premature infants the amount of aspirated amniotic fluid did not vary according to the weight at birth. It is not possible to prove, at least on the basis of these cases, that prematures with a lighter weight at birth aspirate less than those with a heavier weight. When comparing these cases to the corresponding group of fullterm infants, it seems that there is generally less amniotic fluid material in the lungs of premature than in those of fullterm babies.

TABLE 14

Aspiration of Amniotic Fluid in Live-Born Premature Infants under 10 days old
(Cases free from Membranes)

Number, birth weight and age	Aspirated quantity	Symptoms of asphyxia	Complications of labour Post mortem findings
N 788/I/45	Particles ±	—	Subdural hemorrhage
1360 gm	Other subst. ±		
13 min.	Fat ±		
K 970/41	Particles ++		Diaphragmatic
1480 gm	Other subst. +		hernia
30 min.	Fat		
K 2621/45	Particles ±	Born slightly	Polycystic disease of
2080 gm	Other subst. +	asphyxiated	kidneys
30 min.	Fat ±		

Number, birth weight and age	Aspirated quantity	Symptoms of asphyxia	Complications of labour Post mortem findings
N 446/I/45	Particles ±	Born asphyxiated	Ecchymoses
1020 gm	Other subst. ±		
1 hour	Fat ±		
N 852/I/45	Particles ++	Discoloration of amniotic fluid. Born asphyxiated	Ecchymoses
980 gm	Other subst. ±		
2 hour	Fat +		
N 717/I/45	Particles ±	—	Leptomeningeal hemorrhages
2150 gm	Other subst. ±		
9 ½ hours	Fat ±		
N 1043/I/41	Particles ±	Born asphyxiated	Subtentorial hemorrhage
1750 gm	Other subst. +		
18 ½ hours	Fat ±		
K 1019/45 A	Particles ±	Fetal asphyxia	Placenta praevia centralis. Birth of twins.
2430 gm	Other subst. +	Born slightly	
22 hours	Fat ±	asphyxiated	Acute anemia of the fetus
L 26/46	Particles +	—	Subdural hemorrhage
970 gm	Other subst. +		
19 hours	Fat ±		
N 210/II/45	Particles ++	Born asphyxiated	Subdural hemorrhage
1240 gm	Other subst. ±		
23 hours	Fat ±		
L 129/47	Particles —	—	Pulmonary hemorrhage
2000 gm	Other subst. +		
2 hours	Fat ±		
P 172/45	Particles ±	—	Leptomeningeal hemorrhage. Icterus
1300 gm	Other subst. ±		
4 days	Fat ±		neonatorum gravis
P 370/45	Particles ±		Subdural and intraventricular hemorrhage
1270 gm	Other subst. ±		
3 days	Fat ±		
N 463/II/45	Particles ± ?	Born slightly	Pelvic presentation
2180 gm	Other subst. +	asphyxiated	Subdural hemorrhage
6 days	Fat ±		
L 108/47	Particles ±	Born slightly	Purulent meningitis
1620 gm	Other subst. ±	asphyxiated	
7 days	Fat —		
P 76/45	Particles — ?	—	Utero-placentar apoplexy. Congenital hydrocephalus. Serous peritionitis
1300 gm	Other subst. ±		
9 days	Fat ±		

Live-Born Premature Infants. — (Table 14). Particles of the amniotic fluid could be found in the lungs of all who had succumbed within the first 24 hours. Three had an abundant, one a medium and six a samall amount. Strong aspiration was ascertained in the lungs of a premature baby who had survived for half an hour, although one lung was poorly developed, being only about one third of the other (K 970/41). The baby had a shallow breathing from the moment of birth. The cause of death was a large diaphragmatic hernia. Nothing is said as to the course of the delivery which might be taken as a cause of greater aspiration than usual. It can therefore be supposed that even such strong aspiration can occur without any special reason. When comparing this case to another with the same duration of life (K 2621/45), where the post mortem revealed a polycystic degeneration of the kidneys, a considerable difference is noted in the amount of aspiration. The cause of death in this case may be held a total lack of renal function, and the aspiration would then correspond to »normal». — In two cases with a strong aspiration the babies were asphyxiated at birth. In one (N 852/I/45) the aspirated substances were so abundant that they may be regarded to have suffocated the infant (Fig. 26). In the second case, on the other hand, (N 210/II/45) death was due to intracranial hemorrhage. Even in such a case where intra-uterine asphyxia was ascertained, there can be but little aspirated substances in the lung of a baby who survived for 22 hours. (K 1019/45 A.).

If a comparison to fullterm infants is made, it appears that the amount of substances in lungs of premature babies who have died in the course of the first 24 hours, is about the same as in the fullterm. The comparison of the forementioned groups led to the idea that the premature, stillborn and asphyxiated who did not revive, generally had a smaller amount of aspiration than the fullterm. For both these observations to be in harmony with each other it must be supposed, that the disappearance of the amniotic fluid substances occurs more rapidly in the fullterm than in the premature, or that liveborn prematures aspirate as much as fullterm babies.

When making these comparisons it should be borne in mind that only such cases are reported here, where no membranes were found in the lungs. The formation of membranes in the prematures is exceedingly frequent during the first day of life (considerably more

than half of the live-born succumbed within the first 24 hours had membranes). It can be therefore supposed that just these cases who had a strong aspiration, were liable to be affected with membranes. As already said, I have not found it possible to determine the amount of aspirated amniotic fluid in cases with membrane formations, even to such an extent as was feasible where the cases free from membranes were concerned.

In a further examination of prematures with a longer duration of life, a baby two days old (L 129/47) already shows lungs microscopically free from liquor amnii substances. In this case the lumina were full of blood, and this is perhaps why no squamae and cells of the amniotic fluid could be found. In a baby 6 days old (N 463/II/45) only some patches were found, that were probably derived from the amniotic fluid. The particles found in the lungs of a case 9 days old (P 76/45) resembled as to their size the squamae of the liquor amnii, but their determination was uncertain. In prematures of this material I have found no more squamae of the amniotic fluid.

Since the material reported here is limited and it is difficult to conclude on this basis how frequently aspiration of liquor amnii takes place, I have endeavoured, by studying a more extensive material, to form on opinion as to the frequency of aspiration. With this aim in view, I have studied the material yielded by the post mortem examinations carried out by me, in addition to the material

TABLE 15

Aspiration of Amniotic Fluid in Infants who Died under 2 Weeks Age

Age	Number of cases	Amniotic fluid substances in alveoli
0—2 days	Fullterm 46	46
	Premature 52	51
3—7 days	Fullterm 14	11
	Premature 17	14
8—14 days	Fullterm 10	4
	Premature 5	4
Total	144	130

reported here. In part of that material specimens were taken only from one or two lobes, but sometimes pieces taken from all the lobes of the lung have been examined. The material thus obtained has been joined to that which is reported in more detail in this paper. (The cases with membranes are also comprised here). The results are illustrated by table 15. This table contains a great number of cases with sometimes very extensive inflammatory changes.

The Disappearance of the Amniotic Fluid Substances from the Lungs

On the basis of the above I have come to the conclusion that both fullterms and prematures have amniotic fluid substances in their lungs at birth. These substances can be found in the lungs of babies succcumbed in the course of the first week, but later they are found more seldom, and their amount is less.

The question therefore arises, by what ways the liquor amnii substances disappear from the lungs. It is difficult to elucidate it solely by means of post mortem material, as it is not known what was the position and the quantity of these substances in each individual case at the moment of birth. Still, I shall perhaps be able to report some circumstances throwing light upon this subject.

Squamae and Epithelial Cells in the Amniotic Fluid. — Not a single time have I been able to ascertain circumstances speaking on behalf of a disappearance of these particles by absorption. It can be seen in infants a week old that the squamae have changed their shape and are staining less well than in the lungs of babies succumbed in the course of the first 24 hours. As I have studied in this respect only cases free from inflammation, I am unable to say anything as to whether these substances dissolve or are absorbed in pneumonia. Since however they disappear from the lungs in all probability also without inflammatory processes, one easily believes the disappearance to take place in such a way, that the substances pass by respiratory passages into the mouth and from there into the alimentary canal. Leegaard has ascertained in his animal experiments that in rabbits the disappearance of iodipin injected into the nether respiratory passages occurs chiefly by way of the trachea into the alimentary canal, and only a small part of it is absorbed

by the lungs direct, which is a very slow process. These experiments support my supposition that the disappearance of the amniotic fluid substances happens through the trachea. With further reference to LEEGAARD's experiments, one may suppose that such a disappearance is due to ciliary motion, and also takes place without coughing.

Fat. — It is difficult to ascertain when the fat aspirated in the amniotic fluid disappears from the lungs. In fact, the babies often aspirate when sucking milk, and I find it is not always possible to discriminate between drops of fat due to this and fat from the amniotic fluid by means of a microscopic examination. It is however possible to study to a certain degree the appearance of fat outside of the lumina. In some cases drops of fat could be ascertained in the bronchial epithelium. (Fig. 27) They have been demonstrable both in fullterm and premature infants and could be found both in stillborn babies and such as had survived for a few days. If there is an abundant amount of drops, they appear in two rows, one of which is situated basally, and the other in close vicinity to the lumen. Sometimes there are more drops in the basal part than near the lumen. I have not ascertained any proportion between the fat in the lumina and in the bronchial epithelium. Fat was also present in the connective tissue surrounding the bronchioli. On the basis of observations it is hardly possible to maintain, or at least consider it as proved that these findings speak on behalf of a absorption of fat by way of the bronchial epithelium. — In some cases the capillary serum in the lungs was stained yellow by sudan. Sometimes the contents of larger vessels, when stained with sudan or scharlach-R, were of a paler yellow than the contents of capillaries touching them. I feel that such observations support the theory that fat can be directly absorbed into the blood. It seems possible that part of the fat disappears by way of the trachea.

It was not generally possible to establish with any certainty in the sections that the drops of fat or the squamae from the amniotic fluid disappearing from the lungs were amassed in the bronchioli. In case N 352/II/45 on abundant amount of liquor amnii squamae and cells was clearly visible in the »bronchioli», and the corresponding peripheric area contained only precipitate. (Fig. 28) Another place had a similar aspect, the difference consisting in a lack of

contents in the peripheric lumina. In other places of the same section there were unmistakable squamae and cells from the amniotic fluid also in the lumina of the peripheric parts. These observations speak on behalf of the supposition that the substances were withdrawing through the bronchioli after the expansion of the lumina. Such histologic aspets in the section need an abundant amount of amniotic fluid. If the disappearance is slow and the quantities of amniotic fluid small, such forms do not spring into existence, even if the disappearance takes place through the trachea. Consequently, the absence of such observations does not war against my supposition.

Nothing can be said of the disappearance of other substances on the basis of the sections. The precipitate mentioned above probably strongly recedes already after the first few inhalations, so that the same subject can have unmistakably less of it in the extended alveoli than in the smaller »flabby-walled» areas. It does not seem impossible that this substance is absorbed in considerable quantities, but it is evident that it also diseappears throught the effect of respiratory movements. As it is not fully certain whether this substance at all belongs to the amniotic fluid, I feel there is no reason to take up a study of its disappearance.

Taking the amniotic fluid substances together, it can be said of their disappearance that even if part of them are absorbed directly by the lungs, they probably vanish mainly the tracheal way. This theory is further supported by the observation that breathing of even a short duration achieves a great decrease in the amount of the liquor amnii substances — also in such cases where part of the lung is aerated and part has remained congenitally atelectatic. This is especially the case in subjects in whom part of the areas has becom »fully» aerated, and part has remained equally »fully» atelectatic.

Often large cells could be found in the lumen that contained drops of fat and resembled in shape alveolar epithelial cells. The finding of these cells and the circumstance that they contain fat drops does not prove that their fat is a phagocytic one from the amniotic fluid. When performing autopsies I have found in such pulmonary tissue that was entirely unconnected with the lung themselves, a great quantity of cells of the forementioned appearance in the lumen, containing drops which were stained red by sudan (Case L 35/47). It cannot be maintained that in this sub-

ject who was 9 months old, the fat originated from the aspirated amniotic fluid, but it must have come into the cells from other sources. — I do not want to assert on this basis that the alveolar phagocytes should be unable partly to take fat, but to my mind the case clearly proves that there is no need to consider such an occureence as absolutely certain, even if one does find in the lumina fat-containing cells.

Cases Containing Membranes

My material comprises in all 30 cases affected with membranes. With the exception of two cases membranes appeared in infants who survived for less than a week.

TABLE 16

Membranes in Live-Born Infants who Died under 7 Days Age

	Total number	Membranes
Fullterm	18	6
Premature	34	19
Total	52	25

Table 16 illustrates the occurence of membranes in non-inflamed lungs of live-born infants who had died under a week old. As shown by the table, there is a difference between premature and fullterm babies in the frequency of the occurence of membranes. A difference can also be ascertained in the morphology of the membranes. It is therefore advisable to make a separate report on the fullterm and the premature when dealing with the appearance of membranes.

Fullterm Infants

By means of staining fat it was possible to ascertain in a case who died in the process of delivery, that the fat drops had aligned themselves along the walls (Case N 810/II/45). The paraffin section did not reveal any membranelike formations. I do not feel this

could be interpreted as a membrane formation in the same sense as represented below and reported in literature. One baby who had died during delivery had a small amount of membranes (Case N 906/I/46). It was clearly visible how they had originated from squamae. There were also unmistakable transitional forms between the membranes the squamae amassed at the walls. However, it was always possible to distinguish in membranes a distinct lamellar structure — i.e. there were no membranes of a homogeneous substance. The lungs were macrosopically air-containing and the microscopic examination revealed extended tense lumina, which had clearly become aerated. Membranes were found only on the walls of these extended lumina. Another subject who died in the course of the delivery (K 643/45) showed liquor amnii squamae disposed in lamellae along the walls of unmistakably extended lumina. (Fig. 25) This case should be considered an intermediate form of cases with and withbout membranes.

The youngest of the live-born infants in whom membranes were ascertained died not quite five hours old (N 350/I/46). The lumina generally had a small amount of epithelial cells and squamae of the amniotic fluid. Medium quantities of a precipitated substance were revealed by the paraffin section, and fat staining (sudan) showed a moderate amount of fat in the lumina. In some of them a precipitate was found plastered against the wall, where sometimes a dark particle of the size of an alveolar epithelial cell nucleus could be seen, but no other particles. These formations followed the course of the lumen contours, often closely adhering to the walls Their thickness varied. Sometimes a bronchiolus was completely obstructed by this material. These formations could not be found in all the lumina, even the most extended, and in some sections they were only seen here and there on the whole area of the section. There were more of them in sections taken from the left lung, and in the area of the left lower lobe they could be seen in every field. Sudan stained the membranes an orange colour. Membranes were present in the areas of some bronchioli, but the largest quantities were found to the periphery of bronchioli, although not quite in the outermost parts.

Since the mother was affected with diabetes, it is possible that convulsions and cyanosis, as well as accelerated breathing of this

baby were due to hypoglycemia. It appears most probable that hypoglycemia was the reason of the fits described, and the membranes as such did not play any important part as a cause of the primary respiratory disturbances. The amount of membranes was so small that they cannot be considered as a cause of death. At the utmost, they may have been a contributory factor.

Case N 589/II/46 was delivered by a cesarean section and a considerable amount of amniotic fluid was discharged through the mouth after birth. The post mortem revealed a foaming substance in the trachea and its principal ramifications. Macroscopically the aeration of the lungs was scarse and microscopically too, only a few lumina were extended and air-containing. It could be distinctly seen in some places how the precipitate, which stained a pale colour, collapsed against the walls forming membranes. These were nearly homogeneous and contained abundant quantities of fat. They did not show anywhere squamae of the amniotic fluid or other particles. Squamae or epithelial cells of the amniotic fluid were not found in the lumina either. There were in some bronchioli cellular masses staining a dark colour, which seemed to be detached bronchial epithelial cells.

It is difficult to determine in such a case whether the membrane-forming substance in the lumina is aspirated amniotic fluid. The squamae having been so scarse, there is nothing to expose the substance with certainty as amniotic fluid (see above p. 71). The abundant aspiration of amniotic fluid at the moment of birth speaks for the supposition that the substance was amniotic fluid. In this case the blood serum looked the same in microscopic sections as the abovementioned precipitated substance, therefore it cannot be decided on the basis of the histologic preparation that the substance was aspirated amniotic fluid. — Yet taking into consideration the clinical findings, this appears highly probable.

The contents in case N 494/II/45 were both a precipitated substance, as well as skin squamae and epithelial cells. Both were also present as membrane substances. Homogeneous membranes were found, the shape of which did not give any indication as to their origin. (Fig. 29) Membranes abunded in all the specimens, and could also be seen in narrow lumina. There were none in the bron-

chioli, but only to the periphery of these — being present even in the most peripheric parts (See Fig. 15)

Case N 832/II/41 had membranes in several places, mainly in the bronchioli area, but membranes could also be seen in more peripheric parts. The lumina were often full of blood. The origin of the membrane substances could not be ascertained in this case. There were no amniotic fluid substances in the membranes, nor could their presence be established with certainty in any part of the lungs. In some places a few granulocytes could be found in the lumina.

The presentation of this case in the group of subjects free from infection may be erroneous. The possibility must be taken into consideration that the hemorrhages were due to infection. The findings of small quantities of inflammatory cells support this possibility. However, as there were no evident inflammatory symptoms, I have considered the inclusion of this case justified. The microscopic findings in case N 768/I/41 were similar to those of N 832/II/41, some isolated squamae of the amniotic fluid were present in the lumina.

I cannot consider it fully proved that the membranes had the same origin in these cases as in the others. This circumstance is not demonstrable morphologically, as it is not possible to ascertain that membranes are formed by substances in the lumen originated from the amniotic fluid. This is not supported by the fat contents of the membranes, as in cases reported in literature there has been fat in the membranes, in spite of the circumstance that they had been found in adults or so much older children, that there could not be any amniotic fluid substances in the lungs. If however one compares these membranes to those reported in other cases and finds that they greatly resemble each other, it seems probable — when taking the infant's age into consideration — that they have originated from liquor amnii substances also in this case.

Case P 276/45 resembles the two last mentioned. (Fig. 30) This subject had a great amount of membranes, and the lumina were full of erythrocytes. The membranes were thick, rather homogeneous and turned yellow when stained with sudan. They were clearly distinguishable from the tissue below. There were some cells in them, but no particles. Unquestionable amniotic fluid substances were not found anywhere in the lungs. Among the erythrocytes in

the lumen there were a few granulocytes, but no accumulations of them could be ascertained. The lungs had but a few aerated areas. The membranes extended from the bronchi nearly to the outermost periphery. They showed in some places layers of lamellae, and here and there it seemed as if additional substances were accumulating on the membranes. — Also such lumina as were free from membranes, were full of erythrocytes.

Thus, the case is similar to the two previous cases as to the microscopic aspect, but its changes are much more strongly developed. The infant had survived for 13 days and the symptoms had persisted for 11 days. The principal symptom was dyspnea which became gradually worse — finally leading to death. The onset of symptoms so soon after birth and the extension of the microscopically found changes, which is compatible with the supposition that the formation of membranes began simultaneously with the onset of the symptoms, — bring this case into close relation with those, where the substances of the amniotic fluid had formed membranes. It cannot be expected that liquor amnii substances should still be demonstrable in the membranes, even if they had originally been a membrane-forming factor. Although it is supposed that amniotic fluid substances have formed the first membranes, this does not exclude the possibility of a later appearance in the membranes of additional substances, not that new membranes might have originated from these substances.

The character of other fullterm cases with membranes is made evident by table 17.

Premature Infants

In my material membranes in premature subjects were only found in those under 6 days old — they were especially frequent in babies succumbed during the first 24 hours. They did not greatly differ as to structure from the above reported cases. Yet they present some features which are perhaps more characteristic of membrane formations in the lungs of premature than in those of fullterm infants

Not a single time could membranes be ascertained in the lungs of stillborn premature infants. There is one case among the asphyxiated who did not resuscitate, that had membranes (case N 1618/

TABLE 17

Membrane Substances in Fullterm Infants

Number	Liquor amnii squamae and cells	Precipitate	Bronchial or alveolar cells	Indeterminable substances
N 906/I/46 A	+	±	—	-
N 350/I/46	+	+	—	—
N 589/II/46	+	+	—	—
K 965/46	—	+	—	—
L 188/47	—	—	—	+
N 494/II/45	+	—	—	+
N 832/II/41	—	—	—	+
N 768/I/41	—	—	—	+
P 276/46	—	—	—	+

TABLE 18

Membrane Substances in Premature Infants

Number	Liquor amnii squamae and cells	Precipitate	Bronchial or alveolar cells	Indeterminable substances
N 2663/II/45 A	—	±	—	—
N 2663/II/45 B	+	+ ?	—	±
N 930/I/45 B	+	+	— ?	—
N 505/I/45	+		—	-
N 531/II/45	+		±	—
K 423/45 B	±		±	±
K 2188/46 B	±	±	±	±
N 223/II/45	±	—	—	±
L 162/47	—	—	+	+
K 602/46	+	+	± ?	+
L 33/47	—	—	—	+
N 519/II/46 A	+		±	+
N 519/II/46 B	+		±	—
N 519/II/46 C	+		—	—
L 94/46	+		—	—
L 95/46	+		—	+
K 720/45	+		+	—
N 575/II/46	+	?	± ?	+
N 935/I/45	+		—	—
P 203/45	—	—	—	+
N 1618/I/45 B	+	+	—	+

I/45 B, weight at birth 2.360 g.). Macroscopically no aeration could be found in the lungs. In the microscopic section there were unmistakably tense walls that resembled lumina of fully air-containing lungs. These were not seen however in the most peripheric parts. Membranes were abundant and partly formed of a precipitated mass. Amniotic fluid squamae and cells were rare in them. They were found in the tense walls, but also in somewhat more narrow only partly extended lumina could membranes frequently be seen. Blood was abundant in the lumina, and in some places the membranes contained red blood corpuscles.

Two pairs of twins belonging to the group of liveborn prematures had membranes. In addition, there is a set of triplets who all had membranes. Neither of the twins N 2663/I/45 were in a good condition after birth, but the A-baby was worse than the B-baby, and he died sooner than the latter.

The A-baby had a weight of 1.310 gm. at birth and he lived for an hour. The B-baby weighed 1.470 gm. and survived for 14 hours. Leptomeningeal edema was revealed by the post mortem in both cases, but nothing else of interest. The aeration was poor in the lungs of both subjects — B-baby had macroscopically and microscopically more air-containing areas than the A-baby. The latter had a lesser quantity of pulmonary capillaries and a greater amount of cells in the lining than the B-baby. Both had membranes. In A-baby they were present in extended »bronchioli» with tense walls. There were also such »bronchioli» where no membranes were found in the lumina. The substance of the membranes was a precipitate and particles which took on a dark colour when stained and evidently were pyknotic nuclei. (See Fig. 31) (See also Table 18). This mass was also loose in such places of the lumen, where it was small and the wall »flabby». These cells were clearly originated from alveolar lining cells, as intermediate forms could easily be ascertained in them. There were very small quantities of amniotic fluid substances — only some isolated cells of the skin epithelium. The fat staining revealed that the membranes and the said cellular mass were fat-containing. The »bronchial» epithelium had an abundant amount of drops stained red with sudan, arranged in two layers, one at the base and the other in the vicinity of the lumen. More peripherically than these, no fat could be found in the cells.

The B-baby had more amniotic fluid substances in the lungs than the A-baby, although he neither had an abundant amount. Membranes were somewhat more frequent here and their composition was the same as above. Yet some places showed forms which make it probable that membranes are formed by the epithelial cells and squamae of the amniotic fluid — it also seemed that these could produce masses of the same character as described above, perhaps from the proper cells of the lungs. Tinctorially the membranes were strongly fat-containing and there seemed to be some squamae-like particles. There was only a scarse quantity of fat drops in the »bronchial» epithelium and their distribution was irregular. Only part of the extended lumina had membranes. Some of them were such membranes, that their origin could not possibly be determined, as they did not show any separate parts, consisting of a smooth fine-grained substance. These membranes were also fat-containing tinctorially.

The immature twins L 94/46 and L 95/46 both survived for an approximately equally long time (about 7 h.) and both had impeded breathing. Macroscopically the post mortem did not reveal anything but leptomeningeal edema. The lungs of both were only partly air-containing. Microscopically both subjects had a poor aeration, yet it was more extensive in L 95/46 than in its twin. The greater aeration was accompanied by a smaller amount of amniotic fluid substances and simultaneously, less membranes. The difference was not considerable, yet clearly visible. L 94/46 had membranes chiefly on the walls of the tense lumina, but they could be ascertained also on some small lumina with »flabby» walls. The membranes were located in the parts to the immediate periphery of the »bronchioli». (Fig. 32) There were none in the pneumonomeres, nor in the »bronchioli» area. The membranes consisted of the same masses with dark particles as have been described above — it appeared as if these masses were in some places originated by cells which had come off the walls. On the other hand it seemed clear that also the amniotic fluid squamae were plastered against the walls, forming membranes. The membranes were unmistakably fat-containing, with a considerable amount of drops staining yellow with sudan. By means of this staining the membranes stood out clearly from their surroundings, as the other tissues did not contain substances responsive to sudan. The bronchial epithelium was free from fat.

In L 95/46 the membranes were distributed in the same way as in his twin. Morphologically and tinctorially they were also of a similar character. It seemed quite evident that the membrane-forming mass had originated from the liquor amnii squamae, as well as from pulmonary epithelial cells that had become detached.

The weight at birth and age of the triplets N 519/II/46 were as follows:

	Weight at birth	Age
A	1.310 gm.	14 hours
B	1.150 gm.	14 ½ ,,
C	1.080 gm.	29 ,,

It was evident that the C-subject, who survived longest, had the smallest amount of membranes. There were only short bits remaining, which were fat-containing. The membranes consisted, at least mainly, of amniotic fluid squamae and epithelial cells. These substances were also in the centre of the lumen, without having become plastered against the walls. For the main part, the lumina were empty and free from membranes. The A- and B-subjects had more membranes than C. B had most. In both of them the membranes were formed from the squamae of the amniotic fluid, but also epithelial cells that had come off the walls could be found, and they formed the above described mass containing dark particles, being in this way a contributory factor in the origination of the membranes. The position of the membranes in all three subjects was the same as described above for cases L 94/46 and L 95/46.

The C-case had an unmistakably greater aeration than A and B. (See Fig. 33, 34, 35)

Membrane Substances and Position

Fat was a constant finding in the membranes, (Fig. 36) it stained red with sudan and scharlach-R, but Nile blue sulphate had no effect on it, or produced only a pale blue colour. In all cases the Liebermann-Burchard-Schultze reaction was negative in the membrane substances. Not in any single case did they become stained by mucicarmine, at the utmost the edges took on a reddish stain. The maximum effect produced by thionin was a bluish tint

— no metachromic staining could be ascertained. The membranes did not stain in the same way as fibrin, nor was any fibrin-like structure visible in them. BAUER's polysaccharides reaction was negative. The membranes stained yellow with WEIGERT's hematoxylin and VAN GIESON — being sometimes of a homogeneous smooth substance, sometimes on the other hand, lamellae and darker particles could be distinguished. They stained a reddish-purple with DELAFIELD's haematoxylin and eosin. When stained with MASSON's acid fuchsin-aniline blue they took on a strong bluish-purple colour. The membranes were best revealed in the sudan-orange or scharlach-R stainings, as they were then clearly distinguishable from their surroundings — but they were also visible in paraffin sections in all the staining methods employed by me.

When examining membranes, parts are often found, which in all probability have their origin in the detached and partly disintegrated bronchial or alveolar epithelial cells (Fig. 31 Table 17, 18) *) Moreover, substances of the amniotic fluid were of a frequent occurrence. (See Fig. 25.) In addition, there are membranes whose substances it is not possible to specify, owing to the circumstance that they are of a homogeneous or slightly granular nature, where the ingredients cannot be determined with any exactness on the basis of their form and staining (Fig. 29, 30, 37.) — Sometimes the membranes are entirely or partly formed from a precipitated substance. This substance was in fact constantly found in considerable amounts in the lungs of stillborn babies, and its character has already been described. It cannot be distinguished from the blood serum, either morphologically or tinctorially. On the basis of my material I maintain that it is, at least partly, a liquor amnii substance. (See case N 589/II/46 pag 85).

When examining the membrane substances in my cases, it seems that the substance forming them originates from the amniotic fluid, or from detached alveolar or bronchial cells. The fat contents of the membranes do not allow of any conclusions as to their origin. In fact, there are fat-containing substances in the amniotic fluid, but the abovementioned cells also contain a substance staining in

*) In this table the membrane substances are regarded as being alveolar or bronchial epithelium cells only if intermediate forms were present, as explained in the cases reported above.

the same way, which also appears in small drops. There are fat drops in the bronchial epithelium, also in such cases where no loosening or disintegration can be established. Thus, the presence of fat is no help for drawing conclusions as to the origin of membranes. As described in the above cases, it can be seen in the sections how the liquor amnii squamae become plastered against the walls as a membrane. (See Fig. 25.) There are also membranes where the squamae and cells of the amniotic fluid do not have an equally visible shape, but they can still be recognised. It is probable that the disintegration of these substance has altered their shape and one can suppose that this process continues, so that the membranes become homogeneous or nearly so. It is possible in the same way to distinguish intermediate forms between the bronchial epithelial cells and the membranes. When the membranes assume their definite shape, it is often difficult to recognise their origin. Thus, there is the possibility that membranes can be formed by some other substances, besides the abovenamed. I have been unable to determine this with the help of histologic sections. It was moreover impossible to say whether the membranes receive additional substances, e.g. from the blood circulation — but on the other hand, this possibility cannot be excluded on the basis of studies of the sections.

I have found membranes only in such lungs, where respiration had occurred. In them the membranes have placed themselves along the walls of extended tense lumina. Yet they have also been found on such walls of the air-spaces, where the lumen was small an the wall tourtuous. This was found also in the lungs of asphyxiated infants who did not resuscitate. The lumina of these subjects were unmistakably more extended than those found in the lungs of stillborn babies, and the extension of the lumina varies — a mark, on the basis of which I have endeavoured to differentiate between congenital and secondary atelectasis. There were never any membranes in such sections that did not have any unmistakably air-containing areas. — Sometimes membranes also occured in quite narrow lumina (case N 494/II/45), but it is to be surmised that these lumina have collapsed, either intra vitam or postmortally. (Fig. 15.) It must in general be taken into consideration that even if membranes are found in lumina with tortuous walls, the possibility

exists that this tortuousness is due to the collapse of the lung after death. Membranes have been found in the bronchi and bronchioli, and also in the most peripheral parts of the alveolar tree, but they were most frequent, both in fullterm and premature infants, in the areas which lie to the periphery of the bronchioli — but at the outermost periphery (in the alveoli, »Endknospen») they are both rare and scarse. In the prematures, membranes appear just in such pulmonary parts, which have the most extended lumina and tensest walls, and which have the greatest number of capillaries. There were considerable variations in the number of membranes in individual cases. In my material I have also placed such cases into the membrane group, where only a few of them could be ascertained in one single section. In places the membrane was unmistakably coming off the wall and their quantity was insignificant everywhere.

The Relation between Respiratory Disorders and Membranes and their Manner of Origin.

Mention is made in the survey of literature that Farber and Wilson have experimentally ascertained the formation of membranes to be due to forced respiration. It is therefore advisable to examine, to what an extent respiratory disturbances in cases affected with membranes can be ascertained in my material. Information gathered from delivery reports is not always a suitable base for accurate knowledge in this respect about every individual case, as the annotations about the condition of the child are often very short and summary, and in some reports they are restricted to a description of the state immediately after delivery. But part of the reports give minute descriptions of the infant's state. Tables 19, 20 present the respiratory disturbances ascertained on the basis of delivery reports and case histories. The same table also illustrates the post mortem findings and the probable cause of death.

In the fullterm group five subjects had considerable disorders of breathing, which are mentioned in the delivery reports or case histories. Of these five no other cause of accelerated respiration could be found in two cases (N 589/II/46 and P 276/46) than membranes. In the former, membranes were formed of a substance which morphologically could not be indisputably proved as having ori-

TABLE 19

Fullterm Infants Containing Membranes

Number	Respiratory disturbances	Other post mortem findings	Cause of death
N 906/I/46 A	---	Leptomeningeal edema. Adrenal hemorrhage. Renal hyperemia	Adrenal hemorrhage. Died during labour
N 350/I/46	+	—	Hypoglycemia?
N 589/II/46	+	Leptomeningeal edema.	Aspiration of amniotic fluid?
K 965/46	—	Rupture of tentorium cerebelli. Subdural hemorrhage. Congenital hydronephrosis	Intra partum lesion
L 188/47	+	Leptomeningeal edema	Hypoglycemia?
N 494/II/45	—	Congenital hydrocephalus. Congenital heart disease	Congenital heart disease
N 832/II/41	—?	Leptomeningeal edema	Vernix membrane
N 768/I/41	—?	Universal jaundice Adrenal hemorrhage	Icterus gravis neonatorum. Adrenal hemorrhage
P 276/46	+	—	Vernix membrane

ginated from the amniotic fluid, although this seemed probable. In the second case, the character of the membrane substances was morphologically still more uncertain, the baby having survived for such a long time that even had the substances come from the amniotic fluid, it appears improbable that these substances could still be demonstrable. Two cases probably had hypoglycemia, which can be thought to have brought about changes in the respiratory activity — and it can thus be considered that in these cases an extrapulmonary cause had provoked the quickened breathing necessary for the formation of membranes — if we think along the lines of of the abovementioned experiments. In the fifth case (N 906/I/46 A) disorders of breathing can be regarded as due to a complication in the process of delivery — (prolapse of the cord) — the child died during labour. In four cases, where the reports do not make any mention of respiratory disorders, the post mortem revealed in three

TABLE 20

Premature (and Immature) Infants Containing Membranes

Number	Respiratory disturbances	Other post mortem findings	Cause of death
N 1618/I/45 B	——	Leptomeningeal hyperemia. Hyperemia of liver and kidneys. Subepicardial ecchymoses	Intra partum lesion. Aspiration of amniotic fluid. Vernix membrane. (Asphyxiated, not resuscitated)
K 720/45	?	—	Congenital debility
N 575/II/46	+	Leptomeningeal and intraventricular hemorrhage	Idem
N 935/I/45	+?	Leptomeningeal hemorrhage	Congenital debility Intra partum lesion
P 203/45	+	—	?
L 94/46	+	Leptomeningeal edema	Vernix membrane
L 95/46	+	Leptomeningeal edema	Vernix membrane
N 519/II/46 A	+	Intraventricular hemorrhage of brain. Leptomeningeal hemorrhage of medulla oblongata. Leptomeningeal edema	Intra partum lesion and vernix membrane
N 519/II/46 B	+	Leptomeningeal edema	Vernix membrane
N 519/II/46 C	+	Intraventricular hemorrhage of brain. Leptomeningeal hemorrhage of medulla oblongata. Leptomeningeal edema	Intra portum lesion and vernix membrane
N 2663/I/45 A	+?	Leptomeningeal edema	Vernix membrane
N 2663/I/45 B	+?	Leptomeningeal edema	Vernix membrane
N 930/I/45 B	+	Rupture of the liver Hemoperitoneum	Rupture of the liver Hemoperitoneum
N 505/I/45	+	Subdural hemorrhage	Intra partum lesion
N 531/II/46	+	Leptomeningeal edema	Intra partum lesion
K 423/45 B	+?	Serous peritonitis Adrenal hemorrhage	Peritonitis
K 2188/46 B	+	Subdural hemorrhage Subepicardial and thymic ecchymoses	Intra partum lesion
N 223/II/45	+	—	Intra partum lesion and vernix membrane

Number	Respiratory disturbances	Other post mortem findings	Cause of death
L 162/47	+	Subdural hemorrhage of spinal cord. Leptomeningeal edema	Intra partum lesion
K 602/46	+?	Subdural hemorrhage. Subepicardial and mediastinal ecchymoses	Intra partum lesion
L 33/47	+	Leptomeningeal edema	Septicemia?

diseases which can be supposed to have caused respiratory changes, while one case (N 832/II/41) remained unsolved in this respect.

It therefore seems the material tends to prove that in fullterm infants causes often can be found outside of the lungs which may be taken to have provoked quickened breathing, thereby being partly responsible for the formation of membranes. Yet there are cases where no such factors can be disclosed, but the membranes as such have caused the quickened breathing. One sometimes finds in these cases that the difficulties of breathing have set in immediately after birth, and difficult labour must then be considered as having originated the formation of membranes.

In premature infants difficult breathing was observed in the majority of cases with certainty and in the rest with probability. When basing the estimation on the post mortem findings, a great number of cases in this group are such, where no extra-pulmonary factors are revealed that could be regarded as a cause of respiratory changes. The material comprises six cases, in which a macroscopic examination did not reveal anything besides leptomeningeal edema. In addition to them, there were three in which the post mortem examination did not disclose anything of a pathologic nature, besides the pulmonary findings. We must place into the same group the case where nothing was found, in addition to hyperemia of the tissues (N 1618/I/45 B). The disorders of breathing in this case can however be ascribed to circumstances provoked by the process of labour, as the baby died in the course of it. Merely the occurence of pia-arachnoid hemorrhages in the vertex can hardly be considered a significant factor in the origination of quickened breathing (N 935/I/45). In the three remaining cases hemorrhages were found

in the region of the medulla oblongata or in the area of the spinal cord, and these lesions can be regarded as having a significant influence on the respiration. Subdural or intraventricular hemorrhages can also be regarded as such, and they were found in six cases in all. One subject had peritonitis, one rupture of the liver, and one probably sepsis, which can all be factors causing respiratory changes.

It can therefore be said that in about half of the cases of this group quickened breathing was caused by factores outside the pulmonary area, but in the other half no extrapulmonary causes of respiratory changes can be ascertained.

Irregular breathing is found so often in premature infants, that it can be regarded as a constant phenomenon in them, without any other anatomic findings but underdevelopment. The membrane substances in the prematures were of a partly different character than in fullterm babies. In the prematures, one can frequently find membrane substances formed by detached pulmonary epithelial cells, whereas this was not demonstrable in fullterm infants; the question therefore arises whether the tissue changes, due to a premature functioning of the lungs in the former group, have a significant influence on the appearance of membranes. It seems as if, with the onset of respiration, there is a loosening of epithelial cells, both in the central and the peripheral parts of the premature lungs. In all probability, the cell masses, thus detached, take a part in the formation of membranes. When comparing the tissue structure of an immature baby immediately after birth to the lungs of one aged 5 days, it seems that the subject with a longer survival has a considerably smaller amount of alveolar epithelial cells. It is therefore possible that a detachment of cells has taken place here — the mass formed in this way can be supposed to be a causative factor of difficult breathing. Respiratory disturbances can then appear, under the influence of which the substances are plastered against the walls, and membranes originate. In my material immatures are more often affected with membranes than prematures, which speaks on behalf of the theory of their appearance in the prematures and immatures. It is impossible to prove this contention on the basis of the material — and it must be admitted that it has its weaknesses. This loosening of the cells alone does not explain the

appearance of membranes, but I feel it must be taken into consideration as a contributory factor, especially for the immatures.

TABLE 21

Aeration of Lungs in Fullterm Infants Affected with Membranes

No birth weight and age	I		II		III		IV		V		Remarks
	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	
N 906/I/46 A died during labour	+	—	±	—	±	—	±	—	±	—	Ample quant. squamae and precipitate. Moderate quant. membranes.
N 350/I/46 4 ½ hours	++	—	++	—	++	—	++	—	++	—	Moderate quant. liquor amnii particles and precipitateSmall quant. membranes.
N 589/II/46 7 ½ hours	++	—	++	—	++	—	++	—	++	—	Precipitate abundant, particles very scarse.
K 965/46 9 hours	++	—	++	—	++	—	++	—	++	—	Precipitate abundant, liquor amnii particles scarse, moderate quant. membranes.
L 188/47 14 hours	± ?	±	—	±	±	±	±	±	±	±	Moderate quantity membranes. Blood in lumina, small quant. squame.
N 494/II/45 1 day	±	±	±	±	±	±	±	±	±	±	Abundant quant. liquor amnii particles and membranes.
N 832/II/41 5 days											Blood abundant in lumina. Membranes only in bronchi.
N 768/I/41 8 days											Blood abundant in lumina.
P 276/46 13 days											Lumina full of blood Very abundant quant. membranes.

Signs: — no atelectatic areas, ± small atelectatic areas, + middle sizes atelectatic areas which do not comprise half of the area of specimen, ++ atelectatic areas being half or more of the area of specimen.

Ca = congenital atelectasis, Sa = secondary atelectasis. I = right upper lobe, II=right middle lobe, III = right lower lobe, IV = left upper lobe, V = left lower lobe.

Tables 21, 22 illustrate the aeration of the lungs containing membranes. (I have used the same basis of estimation as in tables 7, 10 for the aeration of lungs free from membranes). On these grounds, it is not possible to draw many conclusions as to what an extent the membranes prevent the aeration of the lungs. When

making a comparison with the cases free from membranes, it seems that the aeration was slower in fullterm subjects who had membranes. It is even more difficult to make the comparison for the prematures, nor is there any clearly marked distinction between lungs free from membranes and lungs affected with them. When studying the sections, it can often be found how a membrane seems to obstruct the space between an extended lumen and a narrow one continued from it, — thus it would prevent the aeration of the peripheral part. However, one can also see lumina extended in this way in cases, where no formations of membranes are revealed.

TABLE 22

Aeration of Lungs in Premature Infants Affected with Membranes

No. birth-weight and age	I		II		III		IV		V		Remarks
	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	
N 2663/I/45 A 1310 gm 1 hour	++	—	++	—	++	—	++	—	++	—	Small quant. membr. Small quant. liquor amnii, particles.
N 2663/I/45 B 1470 gm 14 hours	++	—	++	—	++	± ?	++	±	++	±	Small quant. membran. but more than in preceding, liquor amnii particles likewise.
N 930/I/45 B 2220 gm 3 hours	±	±	+	+	+	+	+	+	+	+	Moderate quantity membranes, also amniotic fluid. Several alveoli full of nearly homogeneous substance.
N 505/I/45 1520 gm 3 ½ hours	±	+	—	++	± ?	+	—	++	+	+	Moderate quant. membr., liquor amnii particles scarse. Precipitate in several places.
N 531/II/46 1560 gm 4 hours	+	+	+	+	+	+	+	+	±	+	Membranes are scarse, liquor amnii particles likewise. Moderate quant. precipitate.
K 423/45 B 2050 gm 4 ½ hour	±	±	±	±	+	+	±	±	+	+	Membranes are scarse. Amniotic fluid substances likewise.
K 2188/46 B 2100 gm 5 ½ hours	±	±	±	±	±	±	±	±	±	+	Ample quant. membranes, small quant. liquor amnii particles. Precipitate in several places.
N 223/II/45 2270 gm 8 hours	—	—	—	±	—	+	—	±	±	±	Membranes are scarse, moderate quant. liq. amnii particles.

No. birth-weight and age	I		II		III		IV		V		Remarks
	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	Ca	Sa	
L 162/47 1780 gm 12 hours	±	+	±	±	±	±	±	±	±	+	Membranes are scarse, liq. amnii particles likewise. Small quant. precipitate.
K 602/46 2420 gm 21 ½ hours	± ?	± ?	+	±	±	+	+	+	±	+	Moderate quant. membr. small quant. liq. amnii particles. Ample quant. precipitate.
L 33/47 1380 gm 5 days	—	±	—	—	±	+	±	±	±	±	Membranes very scarse some isolated particles of liq. amnii. Lumina full of blood.
N 1618/I/45 B 2360 gm Asphyxiated, not resuscitated	++	—	++	—	++	—	++	—	++	—	Ample quant.membr Liq. amnii particles likewise. Precipitate and blood abundant.

Signs: Ca = congenital atelectasis, Sa = secondary atelectasis. I = right upper lobe, II = right middle lobe, III = right lower lobe, IV = left upper lobe, V = left lower lobe.

The relations between membranes and breathing and the respiratory difficulties in premature infants during the first days of life are illustrated by the circumstance, that out of the 27 premature live-born infants of my material, who died on the first day of life, only 9 were such who did not show any formations that could be interpreted as membranes. I have considered as affected with membranes all such cases, where formations of this character could be found even in one lobe, therefore there are such cases in this group who had a very small amount of membranes.

Membranes as a Cause of Death

On tables 19, 20 I present the death causes of subjects affected with membranes according to the probability which could be inferred on the basis of post mortem and clinical findings. As illustrated by the table, I have regarded membranes as a cause of death of fullterm babies only in two cases. In the third case (N 589/II/46) the evident cause of death was jointly fetal asphyxia, aspirat-

ion of the amniotic fluid and membranes. As far as all the other fullterm infants are concerned, I feel the membranes cannot be regarded as more than partly responsible for death, or as secondary findings.

With regard to the prematures, I have considered the part played by membranes so great in seven cases, that they can be held responsible for the death at least as a contributory factor of great significance, or taken as the only cause of death. When estimating the cases, I have paid attention to the clinical history, the post mortem findings and the amount of membranes. Even in such cases, where membranes were the only objective finding and the cause of death was clinically unclear, I have not regarded membranes as a cause of death, if they were scarse. In this group there are also cases where the cause of death is evidently another than the membranes, and these are only secondary findings. It is naturally difficult to estimate in every individual case what is the share of the membranes as cause of death, but it is still possible to say that they are secondary findings at least in some cases.

Conclusions. — Membranes originate from the aspirated amniotic fluid, but in all probability, the proper pulmonary cells which come off also have a part in the formation of membrane substances in the prematures and above all in the immatures. In my material membranes are more often found in the prematures than in the fullterms, and possibly more often in the immatures than in the prematures. Often an extra-pulmonary cause of quickened breathing is revealed, but there are also cases, where membranes as such must be regarded as the reason of respiratory disturbances, both clinically and on the basis of post mortem findings. It can be supposed that in such cases the formation of membranes began as a result of difficult labour and aspiration of the amniotic fluid.

Membranes can be regarded as a cause of death only in part of the cases. In addition, they were a contributory factor to the cause of death of some cases. In part of the cases they must be regarded as secondary findings. Approximately in half of the cases affected with membranes these must be considered the principal cause of death, or at least, an important contributory factor.

Thus, the presence of membranes as such is not sufficient to prove that they have caused death, but their amount as well as other post mortem findings and the clinical history must also be taken into consideration. It seems indisputable that membranes can come off and disappear, and therefore they need not necessarily be fatal.

It is probable that membranes for their part can also be a reason of respiratory disorders, and in some cases — the sole reason. Sometimes a *circulus vitiosus* can come into existence, where on the one hand membranes are born as a consequence of respiratory disturbances, but on the other — respiratory disturbances are caused by them, in consequence of which more membranes appear, or the membranes thicken.

Discussion

Fetal State of the Lungs. Intra-Uterine Breathing. Congenital Atelectasis. — As already said, it is impossible to draw any certain conclusions on the basis of post mortem material as to the extension of the lumina in the course of an undisturbed intrauterine life. The process of labour and the exposure to air are factors which must be thought to exercise a great influence on the condition of the fetus, and changes can always take place in the placental circulation that activate the fetus into breathing. Already in a 23 cm. long fetus thoracic movements can be noted when the fetus is removed from the uterus (Minkowski), this can even be the case in a 85 mm long fetus (Windle et al.). It is therefore clear that even when examining quite small fetuses, the lumina microscopically revealed in the lungs can have appeared under the influence of the respiratory movements the fetus made when dying. This must also be taken into consideration when estimating the results of Bender's researches, although he began his examinations on fetuses only 9 weeks old. It is therefore impossible, on the basis of anatomic findings, to furnish any conclusive proof of the presence of lumina in the lungs in the fetal state. Since a determination of intrauterine breathing by means of histologic sections is based on the findings of extended lumina, it must be admitted that it is hardly possible to ascertain any intra-uterine respiratory activity on the basis of antomic observations. It is equally difficult to settle the question of a physiological aspiration of amniotic fluid in the fetal state, which is closely connected with the size of the lumina and intrauterine breathing, in the light of anatomic observations. According to my material it is possible to say that evidently newborn infants have liquor amnii substances in their lungs. This does not prove that it was so in the fetal state.

X-ray examinations of human fetuses do not yield any conclusive evidence with regard to intra-uterine breathing and aspiration of the amniotic fluid, as the possibility is also present here that the fetus had aspirated in consequence of the manipulations. Yet the positive results obtained with them have in my opinion a greater power of evidence than anatomic observations, and if their results are compared with those of animal tests, it appears highly probable that the human fetus aspirates amniotic fluid in utero. The occurrence of intra-uterine respiratory movements must now be regarded as proved on the basis of researches made already by Ahlfeld, and of late by Snyder and Rosenfeld as well as Bonar.

In my own material, the lumina always found in the fetal lungs and the amniotic fluid substances present in the lungs of nearly all newborn infants, also speak in my opinion on behalf of intra-uterine breathing, even if I cannot consider them as any conclusive evidence. If it is now admitted that the fetus breathes in utero and physiologically aspirates amniotic fluid, it is hardly logical to suppose that this latter will stop in the trachea. Moreover, the roentgenography contrast medium did reach the lungs in the experiments made with human fetuses (see p. 20 in the survey of literature). Even if it must be taken into consideration, that this aspiration may be artificially induced, it must be admitted on the other hand, that corresponding stimuli can have their effect on the fetus also in an undisturbed intra-uterine existence, due to contractions of the uterus (Szendi). If the fetus aspirates amniotic fluid down to the pulmonary tissue, it follows that lumina must be found also in the pulmonary tissue, nor are the walls in close contact to each other in the fetal state. In my material unmistakable lumina were to be found everywhere in the pulmonary tissue, both in the lungs of kittens killed in utero, and in the human fetuses who had died during pregnancy or in the birth process. The sizes of the lumina were similar in the lungs of the cat fetuses killed in the same manner, but in the fetus that was suffocated intra-uterinally by aspirating amniotic fluid, the lumen was clearly larger. There were considerable variations in the lumen size in the lungs of fullterm human fetuses. This was evidently dependent upon how much the fetus had aspirated during pregnancy or labour. The variations were great

also in such cases where a compression of the umbilical cord was ascertained. The size of the lumina is not probably solely determined by the potency of the factors provoking respiratory movements during labour or pregnancy, but also by other factors as well — during labour e.g. by the quantity the fetus is able to aspirate. It is of course natural, that a fetus whose mouth — during the compression of the umbilical cord — is strongly pressed against the walls of the genital passages, or if his thorax is compressed by them — cannot aspirate to the same extent as a fetus who has his mouth and thorax free. In all probability the extension of the lumina is determined by other factors also, because this is not sufficient in itself to explain the variations of the lumen size in my material.

It is not possible to determine with the help of my material, to what an extent the lumen sizes vary physiologically. If the fetus respirates amniotic fluid in utero in and out, this also presupposes variations in the sizes of the lumina. I feel that we must regard as »normal size» of the fetal lumen the smallest size which can be found in the post mortem material. The lumen ratio in the histologic section of the lungs of a fullterm fetus is then 15 % of the whole area counted in one dimension. The lumina of premature fetuses are, according to my material considerably smaller. They vary in fetuses of a different weight, having a minimum of 5 %. They are also visible in this case, but are so small that the walls touch one another in places.

The fulltime fetuses of my material have considerable variations in the sizes of their lumina. As a rule, the lumina of specimens taken from different lobes of the same lungs are about the same size. According to animal experiments, the dilatation of the lumina in the lungs of the cat fetus killed in utero is more or less uniform in the different parts. With the dilatation of the lumina, the pulmonary structure remains otherwise unchanged. As already said, considerable changes were revealed in different cases also in the lungs of the human fetus. Yet their other characteristics were similar. There were intermediate forms between the highest and lowest lumen ratio. It would therefore be an artificial idea if a certain lumen size did not belong to congenital atelectasis. Nor does it appear reasonable to describe as congenital atelectasis only such

cases which do not have any lumen — irrespective of the point of view one adopts in regard to the lumen size in the fetal state. In that case the result would be that the lungs of a stillborn fetus would exceedingly seldom — if ever — be congenitally atelectatic, even if it had not inspirated any air. The simplest course to adopt in determining congenital atelectasis is to revert to Jörg's original determination. According to it, lungs are (congenitally) atelectatic as long as they have not yet expanded under the influence of air. Therefore the size of the lumen in congenitally atelectatic lungs can vary in different cases. Congenital atelectasis is then not identical with the fetal state of the lung, but I feel that this determination is better adaptable in practice and seems to correspond better to our conception of the nature of congenital atelectasis than in case the size of the lumina is used as a standard for determination. In addition, there is the advantage that this determination does not, when speaking of congenital atelectasis, demand any definite attitude with regard to the fetal state of the lung — above all, the size of the lumina ante partum.

Aspiration of the amniotic fluid should according to the above, be assessed in conformity to the extension of the lumina. However, this can only be said provided the lumen does not have any other contents than amniotic fluid. Yet this circumstance is not self-evident. The animal tests revealed that the lumina of the cat fetus regularly had cells which looked like epithelial cells, with a great number of vacuoles. Corresponding cells were found in the lungs of the human fetus. In addition there was, especially in the latter, a regular and constant finding of a precipitated substance which was often the principal contents of the lumen. This substance is probably, at least to the greatest extent, amniotic fluid, but it could not be proved as such on the basis of its morphologic and tinctorial characteristics. If it is not regarded as amniotic fluid it must be surmised that it has been aspirated from the genital passages or is a product of the lungs themselves. It may be a result of glandular secretion or a residue born in the process of the evolution and growth of the lungs. The circumstance that epithelial cells that have evidently come off the walls are found in the lumen, speaks on behalf of the theory that their disintegration can be partly responsible for the formation of this substance. It was some-

times possible to demonstrate in this mass that a very small part of it stained red with mucicarmine,whereas there was simultaneously in the bronchial glands a considerable quantity of substances, staining in the same way. This supports the surmise that part of the substance can be mucus, born as a result of the secretion of the bronchial glands. If the substance has originated in the lungs, it means that its disappearance necessitates a flow from the lungs in the direction of the trachea. This flow need not be a consequence of inta-uterine respiratory movements, as it can be surmised that the cilial motion alone would be sufficient to remove the substance. Cases in which a congenital larynx atresia was found, and simultaneously widely expanded lumina in congenitially atelectatic lungs, filled with mucus (Frankenberg, Kovacs) bear out the theory that there is normally a flow of substances from the lungs into the amniotic fluid. The presence of epithelial cells and squamae from the skin is a much surer sign of aspiration of liquor amnii than this precipitated substance and it is easier to determine their quantity. Even if these quantities vary in the amniotic fluid, presenting in individual cases different pictures of the extent of the aspiration, I consider their determination to be the surest method of assessing the extent of the aspiration. There are difficulties in estimating the quantity of »physiologic» aspiration; this type of aspiration is best represented in a case, where the process of labour has as little influence as possible on the fetus. In the fullterm fetus who had the smallest lumina in the material, the aspirated quantity was rather abundant and appeared in all the lobes. If the smallest determined quantity is taken as a standard for physiologic aspiration, particles of the amniotic fluid are found in every lobe, although their quantity is insignificant. In that case the quantity of cells and squamae is so small that the amniotic fluid filling the mouth of the fetus, can be surmised to be sufficient for it. In my material the aspiration is generally smaller in premature than in fullterm infants, in accordance with the smaller size of their lumina. — It is possible that the extent of the physiological aspiration also varies. It is also possible, within certain limits, to estimate the extent of intra-uterine asphyxia on the basis of the expansion of the lumina in congenitially atelectatic lungs, but in cases where air has already entered the lungs, this is no longer possible. The amount of aspira-

ted substances can then give an idea of the extent of aspiration. There are cases in my material revealing evident intra-uterine asphyxia and a small quantity of aspirated substances, and on the other hand, cases with no signs of intra-uterine asphyxia and abundant amounts of aspirated substances. In order to be able to understand these cases we should, I feel, support to a certain extent the explanation given by SCHULTZE, according to which transient intra-uterine asphyxia can be the cause of aspiration and, on the other hand, a slowly and gradually appearing oxygen want which does not cause aspiration. Thus, it is not always possible, on the basis of the amounts of aspirated liquor amnii substances, to draw definite conclusions as to whether the infant was born asphyxiated or not. However, it seems that such exceptions are rare. The impression is gained from my material, that as a general rule, strong aspiration is a mark of intra-uterine asphyxia — especially such as has occured during labour or its final stages but that, even if the fetus was clearly asphyxiated, abundant amounts of aspirated amniotic fluid are not always found in the lungs. It is of course evident that the amount of aspiration is influenced partly by the same factors as the extension of the lumina (see above). It is therefore difficult to determine when the aspiration must be regarded as pathological, in the sense that it is an indicator of fetal asphyxia. Thus, my material seems to demonstrate that there can be a moderate or even insignificant aspiration, though the fetus was asphyxiated. The »physiological» aspiration is quite small. The division between these conditions is difficult to draw, still less can any figures be stated according to which it would be possible to determine the amount of aspiration as an indicator of asphyxia. Yet it is possible to say that, without any special causative factors, aspirated substances are found in all the lobes of the lungs of infants born at term. The amounts are often smaller in prematures, and substances may be found only in some parts of the pulmonary lobes.

Aeration of the Lungs and Pulmonary Factors Influencing it. — Post mortem material has its limitations with regard to the estimation of aeration. The collapse of the lungs which sets in postmortally can greatly change the intra vitam aspect. As already mentioned it is, notwithstanding, possible to draw conclusions

on the basis of my material, the methods of procedure having been identical in all cases. In my animal experiments I have endeavoured to restrict the postmortal changes to the minimum, because in them a comparative quantitative estimation was made of the aeration in different cases. In my post mortem material I have drawn no conclusions on the basis of measuring the extent of the lumina. My sole endeavour was to determine by examining the section, whether some area had ever been air-containing. In this respect an aerated area and one affected with secondary atelectasis are equivalent. In microscopic sections, it may be a matter of interpretation as to when some area is to be considered as having become atelectatic. It was demonstrable in the animal tests that unmistakable lumina could be seen microscopically even in such lungs of kittens, which macroscopically appeared completely airless and did not float, only part of these lungs being completely deficient in lumina. The post mortem material shows intermediate forms, from widely extended lumina to a nearly complete deficiency in them. In determinations of atelectasis a completely airless condition is often mentioned (see p. 14), but in addition, also a decrease of aeration (Bergstrand). For secondary atelectasis mention is made of the possibility of contents in lumina (Hanson and Sjöstrand), these contents having the appearance of edema fluid. In atelectasis caused by compression I have found in macroscopically completely airless lungs of infant 4 months old, that a microscopic examination revealed clear though excedingly small slitlike lumina. — If the concept secondary atelectasis is to be confined within the same limits as congenital atelectasis, airlessness must be regarded as one of its characteristics. This, as explained above, does not mean the same thing as a complete absence of lumina. Microscopic sections can reveal empty lumina, if the contents are such that they do not fix. But some empty or nearly empty lumina can also be seen in congenital atelectasis, though it is evident that no air has entered the lungs. There are borderline cases in both groups, where it is difficult or even impossible to estimate whether a certain lumen is atelectatic or air-containing.

As already mentioned, the determination of the concept secondary atelectasis has no significance for the results of my researches. Atelectatic areas were demonstrable in all the cases examined by me.

Even if possible postmortal changes are disregarded, small atelectatic areas cannot be considered as evidence of a pathologic state, as it is most probable that there are also some physiologically airless collapsed areas in the lungs, — as it was proved by VERZAR's and JEKER's animal experiments.

A determination of the aeration of the lungs in accordance with the disappearance of congenital atelectasis harbours, in addition to the difficulties of interpreting the sections, also some possibilities of errors. Theoretically it is possible that some area can collapse and take on the aspect of secondary atelectasis without having become aerated in between. My animal experiments argue against this possibility, but as they could be made use of only if carried out with kittens a few hours old, they do not eliminate the possibility of such a state of things in subjects with a longer term of life. On the other hand, the structure of lungs affected with secondary atelectasis can alter so that the epithelium becomes regularly isoprismatic, which makes it difficult to differentiate them from congenitally atelectatic lumina. This can happen, according to MOULONGUET's test, in dogs already within 6 days. It is difficult to determine with what rapidity such changes take place in the newborn. In my opinion, this should be taken into consideration when determining, on the basis of morphologic characteristics, the extent of respiratory activity in the lungs of infants several weeks old. It is possible that this circumstance is responsible for the erroneus conclusions published in literature with regard to the persistence of congenital atelectasis.

It seems that animal experiments do not justify conclusions as to how rapidly the aeration progresses in man. Although there is no considerable difference in the structure of lungs of kittens and newborn infants, that of the former being however somewhat more simple, there is such a great difference in the vitality, that there are reasons to surmise a quicker aeration in kittens than in newborn infants. This being so, the circumstance that the lungs of kittens were already fully air-containing one hour after birth does not by any means justify the contention that this is the case in human lungs. On the other hand, it must be taken into consideration that when examining the lungs of infants who had died in hospital,it is not possible as a rule to obtain for examination

a baby a few hours old, who had been brisk and breathed well the whole time.

I have endeavoured in my experiments to make clear how quickly the lungs can become aerated. If the question is posed thus, different results are arrived at than when attempting to determine, how long congenital atelectasis can persist. It is therefore evident that my material yields different results than the researches of Farber and Wilson, based on an extensive material. The impression is gained from my material that a few inspirations suffice to bring about an expansion including the outermost periphery in lungs of fullterm infants, although this is not demonstrable by post mortem examinations in all parts of the lungs, some parts remaining atelectatic. Therefore it is not possible to deny, on the basis of post mortem material, that the lungs of a brisk infant breathing well may become fully aerated in the course of the first few hours. This evidence was not to be found in my own material, the aeration having been slow in my cases. Still, it can be maintained on the basis of my material that the expansion is not a matter of weeks, but days — not excluding premature or even immature infants. According to this, the aeration is somewhat more rapid in fullterm than in premature infants, and I have come to the conclusion, in the light of my material, that the expansion of the fullterm lung takes two-three days, which conforms to the results of Farber's researches. The lungs can also become areated in prematures already after a few indrawn breaths, but this was only demonstrable in limited areas comprising at the utmost the areas of one lobe — i.e., clearly less than in fullterm babies. A breathing of five days duration has been sufficient for an aeration of all parts of the lungs of a premature infant under 1000 g. of weight. I do not wich to deny the possibility that congenitally atelectatic areas can persist for weeks in a premature lung (Farber and Wilson), but I feel it can be assumed in that case that there might have been factors exercising a restraining influence on the aeration, which cannot be detected anymore in a post mortem examination.

Therefore, although it is sometimes possible to observe an aeration including even the most peripheric parts, post mortem findings in the lungs of both fullterm and premature babies succumbed in the course of the first few days of life show the aeration to have

been such, that the outermost periphery has retained its small lumina, whereas the central parts of the alveolor tree became fully air-containing. This state can be met with also in cases which have become secondarily atelectatic. It is therefore conceivable that this has appeared postmortaliy, after the collapse of the lungs. Such a possibility cannot be completely disregarded, but the circumstance that vernix membranes were as a rule found solely in these expanded places, strongly argues in favour of the surmise that these formations appear *intra vitam*. Nobody ever reported having found vernix membranes in babies who had not breathed air, and in my own material membranes were only met with in aerated lungs.

The different rapidity of aeration in different pulmonary areas can be related to the various stages of their development. This is borne out to some degree by the different state of development of the elastic tissue in distinct parts of the lung. (See SETÄLÄ).

Since post mortem examinations invariably demonstrate amniotic fluid substances in lungs of babies under three days old, and since it appears probable that all newborn infants have liquor amnii in their respiratory passages, this factor must be taken into consideration as possibly exercising an influence on the aeration of the lungs. »Physiological» aspiration does not seem to have any special significance in this respect. The circumstance that the expansion is slower in the periphery than in the central parts can be due to some extent to the aspiration of amniotic fluid. It is often visible in the sections how the peripheric narrow lumina are filled with substances, that are partly unmistakably, partly probably, liquor amnii substances. It is therefore conceivable that, with the rush of air into the lumina, the amniotic fluid in them withdraws towards the periphery and disappears gradually, partly under the influence of respiratory movements and partly through absorption. Then only do the peripheric parts also become aerated. It is evident that air can penetrate also down to the periphery and the amniotic fluid substances become plastered against the walls of the extended lumina. Depending on the amounts of amniotic fluid and the character of the respiratory activity — perhaps also on the nature of the amniotic fluid — its substances remain in the walls for a short time and disappear already with the following breaths, or the substances adhere to the wall and form vernix membranes. If the as-

piration is abundant, it can result in suffocation without any formations of membranes. Some areas can be so full of amniotic fluid substances, that air cannot peretrate them at all. However, the lungs become partly aircontaining in such cases, even if there are abundant amounts of liquor amnii in the trachea, and I feel that we can speak of suffocation by amniotic fluid only provided aeration can be ascertained. An intra-uterine suffocation by amniotic fluid is only the result of completely illogical thinking.

With the gradual withdrawal of the liquor amnii substances from the lungs, it is conceivable that after the cleansing of the pharynx and larynx, these substances can again be found in the upper respiratory passages. This is not therefore necessarily a formation of mucus due to irritation of the respiratory passages. It cannot be denied of course that mucus can be secreted in consequence of an irritation by foreign substances. In my material, mucus could be demonstrated tinctorially in small quantities in the deeper parts, but there was often more of it in the bronchial glands and mucous membrane — yet never in any significant quantities. Thus, in the light of this research, the substances found in the neonatal lung are mainly liquor amnii substances — also however containing such, whose origin it is difficult to determine.

Elements from which membranes result are mainly amniotic fluid, at least in fullterm infants. To produce these membranes, aspiration exceeding the quantity of »physiological» aspiration is necessary. Intra-uterine asphyxia is not a constant finding, by which the abundant aspiration could be explained. It can be surmised that it is a result of earlier transient intra-uterine asphyxia, or it can have occurred at the final stages of labour, so late that there was no time for the symptoms of asphyxia to appear during the process of labour. My material does not contain cases which could lead me to suppose, that the amniotic fluid substances concentrate in the walls of the lumina already during intra-uterine existence (comp. ERHARDT's x-ray researches, p. 24). According to my material, the membranes in prematures often contained cells detached from the walls of lumina, which had undergone changes — disintegrated into a partly structureless substance before they had formed membranes. A similar mass can sometimes also be formed by amniotic fluid substances. It is therefore conceivable that such masses had origi-

nated solely from amniotic fluid substances. I feel however that I have been able to ascertain intermediate forms, from detached cells to complete membranes. I therefore consider that my material makes it evident that cells detached from the walls also play their part in the formation of membranes in premature infants. For fullterm babies, I have been unable to conclusively ascertain such forms, but in one case there were observations pointing in this direction. Therefore, I do not consider that the formation of membranes in fullterm and premature infants is necessarily different. In prematures membranes also clearly result from amniotic fluid substances. There is every reason to maintain the name *vernix membrane*, since the part played by the amniotic fluid in the formation of membranes is most evident and conclusive. The formation of membranes does not presuppose any inflammatory processes, as membranes were often present in lungs without any signs of inflammation. In connection with another research of mine I have found that membranes do not occur more frequently in pneumonic than in noninflammed lungs. Taking into consideration the high incidence of membranes in my material, it is evident that they also have a clinical significance. They can appear in such small amounts that they do not seem to involve any particular respiratory disturbances, but in some cases they are present in such abundant quantities, that they are the only cause of death according to the post mortem examination. My material makes it evident that membranes appear simultaneously with the first indrawings of breath. Therefore their occurence should be taken into consideration when looking for the cause of difficult respiration on the first day of life. Still, membrane formations can be the cause of respiratory disturbances continuing for several days. In such cases it could not be proved that membranes had originated from the amniotic fluid substances. It is possible that membranes can appear in the newborn without any relation to aspirated liquor amnii. It is however certain that the main part of membranes in the newborn are formed from the amniotic fluid substances, and if there are membranes resulted in a different way, they are a most uncommon occurrence.

There is not a single membrane case in my material with necroses in the walls. The walls covered with membranes have not shown any different structure than the areas free from membranes.

In the light of microscopic sections, it appears that membranes prevent the aeration of the lungs. When a comparison was made between the groups of cases affected with membranes and free from them, the difference was not clearly visible. Examinations of twins and especially triplets provide a strong argument in favour of the surmise that the amounts of membranes are significant, both with regard to the duration of life and to the aeration of the lungs. Considering the position of the membranes, it is quite natural that they are a most significant factor, especially in prematures, impeding the exchange of gases. They occur most frequently in fact just in those parts where the greatest quantity of capillaries contact the lumina and which have become air-containing. In this way the membranes injure the oxygen supply, difficult of itself in premature infants. According to my material, vernix membranes are the most important (non-inflammatory) pernicious result of the aspiration of amniotic fluid.

Summary

Definite conclusions about intra-uterine breathing and the fetal state of the lung cannot be drawn solely on the basis of post mortem material and histologic examinations of lungs of animal fetuses — especially with regard to whether there are lumina in the lungs and how much they are extended already during intra-uterine existence. Lumina in the fetal lung were found in every instance but no evidence can be produced that a corresponding state prevails in an undisturbed intra-uterine existence. The lumina expand during fetal aspiration of the amniotic fluid, if the placental circulation is disturbed or interrupted. This was fully demonstrable in the animal experiments, and the post mortem material argues in favour of the surmise that this also is the state of things in the human fetus. Thus, the extension of the lumina in the fetal lung is some kind of a standard for measuring the extent of intra-uterine asphyxia.

In determining congenital atelectasis, it is best to revert to J ö r g's original determination, according to which the lungs are congenitally atelectatic as long as they are not expanded through the influence of aeration. Post mortem examinations of congenitally atelectatic lungs always reveal lumina, and their sizes vary considerably, although the structure of the lungs remains otherwise unchanged. The lumen size is approximately the same in different places of the same lung. The smallest lumina were found in premature fetuses.

In the light of post mortem material, amniotic fluid is always to be found in the neonatal lung, which enables us to speak of a »physiologic« aspiration of the amniotic fluid. The amounts however usually appear small. The extent of the aspiration can vary in individual cases, without any reason being demonstrable for a stronger aspiration than usual. Small amounts of aspirated amniotic fluid have no noxious effect on the newborn. A strong aspiration can result in suffocation, in which

case the lungs become partly air-containing. Fullterm infants aspirate more than prematures, although abundant aspiration can sometimes also be found in the lungs of the latter. Vernix membranes are a comparatively frequent finding in the neonatal lung; they are formed mainly from amniotic fluid substances, but at least in premature infants, they can partly result from disintegrated cells which have become detached from the walls. These membranes are found only in aerated lungs, though they can be present in the lungs of babies who had died during labour. They must be taken into consideration as a cause of neonatal death, and are only revealed by a microscopic examination.

In the light of the material on which post mortem examination can be made, the process of aeration is gradual in both fullterm and premature infants. It is more rapid in the fullterm than in the premature, but the material does not disclose any considerable difference, since the process of aeration lasted for 2—3 days in the fullterm, and was complete in the premature lungs already of the 5th day of life. It seems however that a few breaths are sufficient to result in an almost maximum aeration of the fullterm lungs. The possibility cannot therefore be denied that the lungs of a fullterm infant with good breathing may become fully air-containing already in the course of the first day of life. This is much less probable with regard to the prematures. According to the post mortem material, the expansion of the lungs with air occurs in such a way, that the central parts of the alveolar tree are the first to expand, after which the outermost periphery gradually becomes air-containing. As an exception, the expansion can take place in some lungs in the whole area of the alveolar tree. The manner of expansion is the same both in premature and fullterm infants, although it is better visible in prematures, especially in the smallest babies, since the periphery becomes areated more slowly than in the fullterms.

The expansion can be delayed by aspirated amniotic fluid and vernix membranes.

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ILLUSTRATIONS

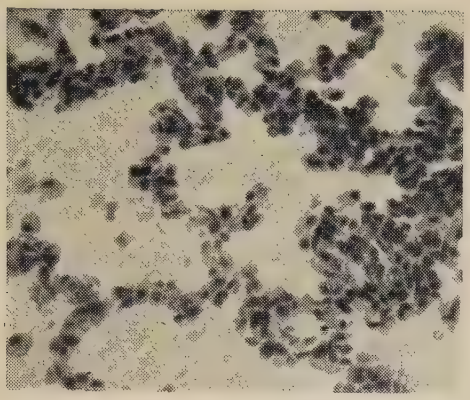

Fig. 1. Congenitally atelectatic lung of cat, with a lumen ratio of abt.50%, Walls are tortuous, lumina almost empty. (Cat 11/I, upper part of right lung. Hematoxylin and van Gieson. × abt 200.)

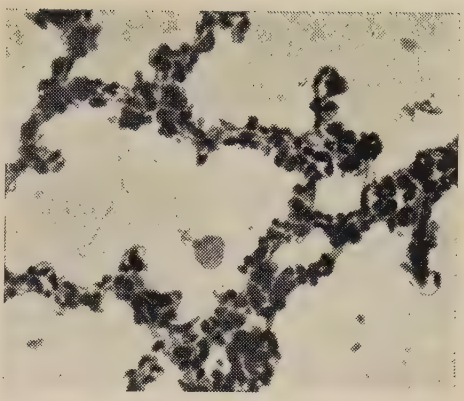

Fig. 2. Lung of cat suffocated in utero, with a lumen ratio of abt. 60 %. Walls are straighter than in preceding case. Small amounts of contents in lumina. (Cat 10/II. Hematoxylin and van Gieson. × abt 200.)

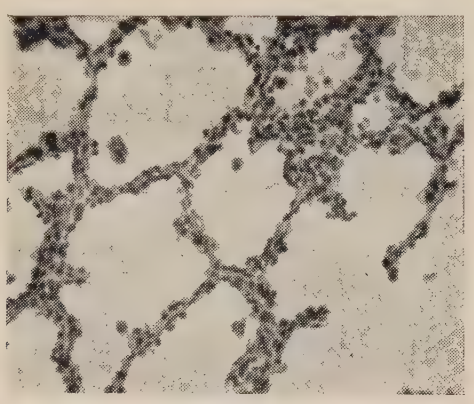

Fig. 3. Lung of cat which inhaled some air. No essential difference as compared to fig. 1 and 2. (Cat. 7/III. Hematoxylin and eosin. × abt 200.)

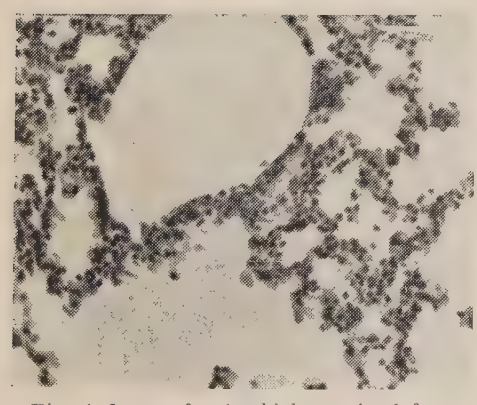

Fig. 4. Lung of cat which survived for an hour. The figure clearly illustrates the tension of the wall in an aerated area. (Cat. 6/I. Hematoxylin and van Gieson. × abt 200.)

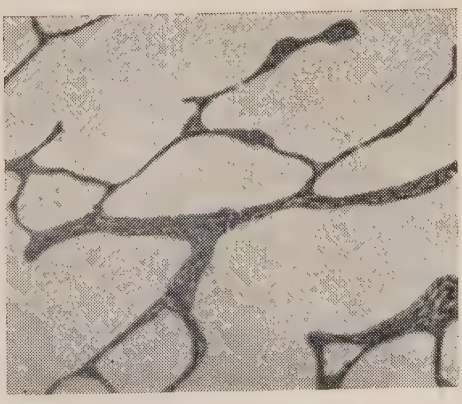

Fig. 5. Lung of cat which survived for 42 hours. All lumina visible in the fig. are air-containing and the pulmonary structure clearly differs from that of a lung with congenital atelectasis. (Cat 8/II. Hematoxylin and muci-carmine. × abt 100.)

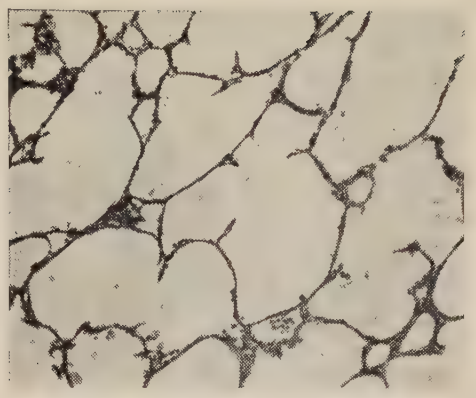

Fig. 6. Lung of cat surviving for 45 minutes, which is fully aerated. Walls are thin and »tense». (Cat 11/II. Hematoxylin and eosin. × abt 50.)

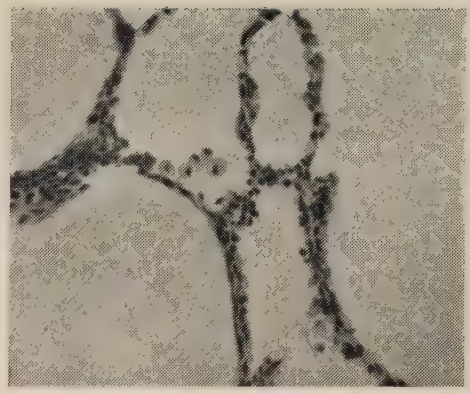

Fig. 7. Same as in fig. 6. × abt 200.

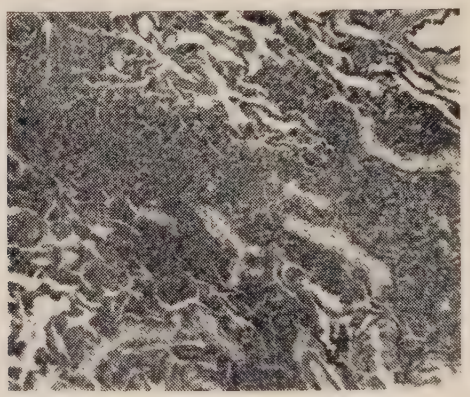

Fig. 8. Lung of cat with secondary atelectasis. Lumina are to be found only in the peripheral parts of the fig. The tissue in the central parts is deficient in lumina. (Cat 7/II. Hematoxylin and van Gieson. × abt 50.)

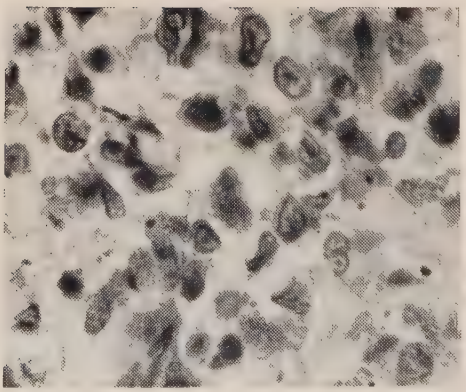

Fig. 9. Lung of cat with secondary atelectasis. The tissue has no lumina. (Cat 1/V. Hematoxylin and van Gieson. × abt 900.)

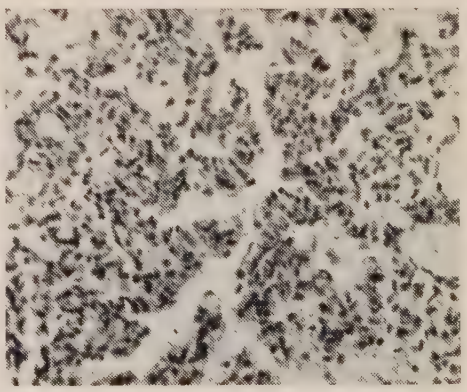

Fig. 10. Lung of cat with secondary atelectasis. Narrow lumina. (Cat 1/V. Hematoxylin and mucicarmine. × abt 200.)

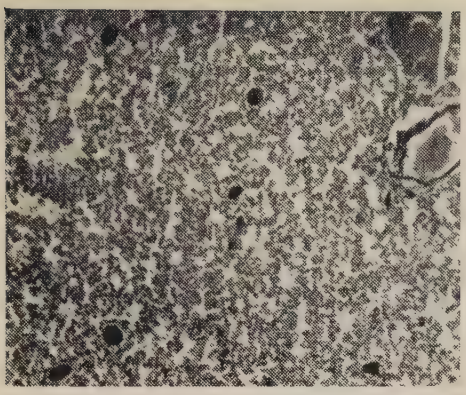

Fig. 11. Lung of fetus with congenital atelectasis. The fetus was born asphyxiated and did not resuscitate. Small lumina, tortuous walls. (Case N 979/I/46. Birth weight 2980 gm. Hematoxylin and eosin. × abt 50.)

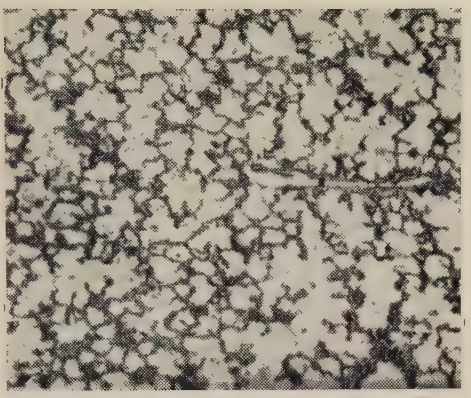

Fig. 12. Lung of fetus with congenital atelectasis, with unmistakably larger lumina than in fig. 11. Abundant contents in the lumina. Fetus died in the course of delivery. (Case N 810/II/45. Birth weight 3300 gm. Masson's staining. × abt 50.)

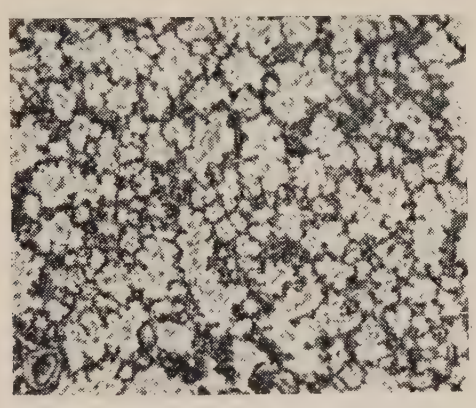

Fig. 13. Lung of fetus with congenital atelectasis, where the lumina are of abt. the same size as in fig. 12. The lumen ratio was clearly different in these cases. (Table no. 5). This difference is due to the different thickness of the walls. (Case N 2686/II/45. Birth weight 3000 gm. Haematoxylin and eosin. × abt 50.)

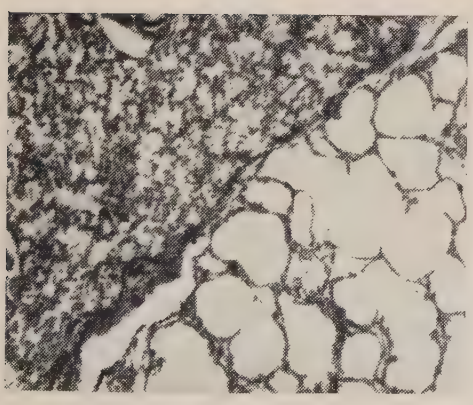

Fig. 14. Partly congenitally atelectatic,partly aerated lung. The borderline between these areas is pronounced. Fullterm fetus who died during labour. (Case K 719/45. Birth weight 3750 gm. Masson's staining. × abt 50.)

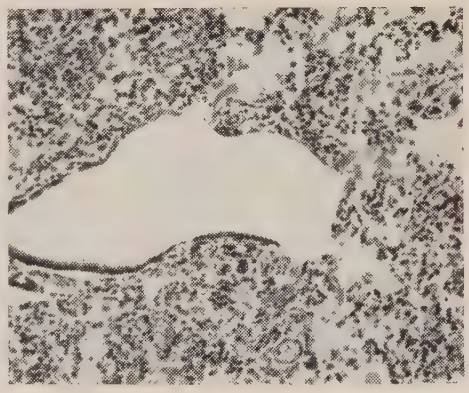

Fig. 15. Partly aerated lung of infant who survived for 24 hours. The outermost periphery is not aerated. Abundant amounts of vernix membranes. (Case N 494/II/45. Birth weight 2870 gm. Hematoxylin and eosin. × abt 100.)

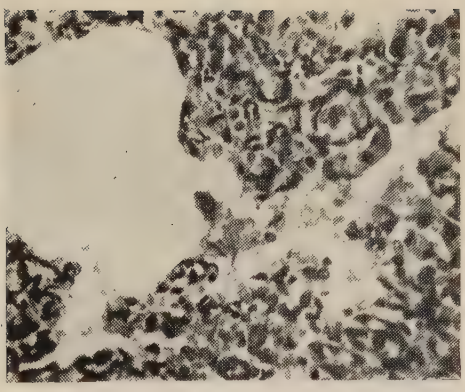

Fig. 16. Same case as Fig. 15. This case had abundant membranes. The fig. does not illustrate areas affected with membranes. It is clearly visible that the outermost periphery is not aerated. × abt 300.

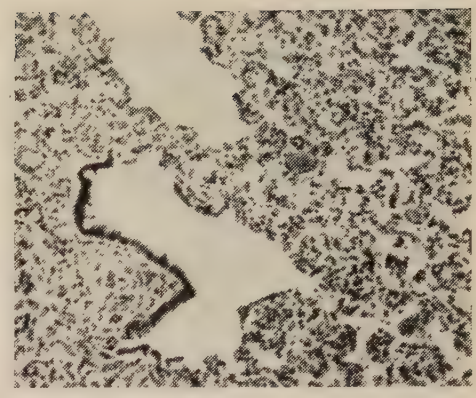

Fig. 17. Pulmonary tissue which has become partly air-containing. Fullterm fetus who was born asphyxiated, not resuscitated. (Case N 979/I/46. Birth weight 2980 gm. Hematoxylin and van Gieson. × abt 100.)

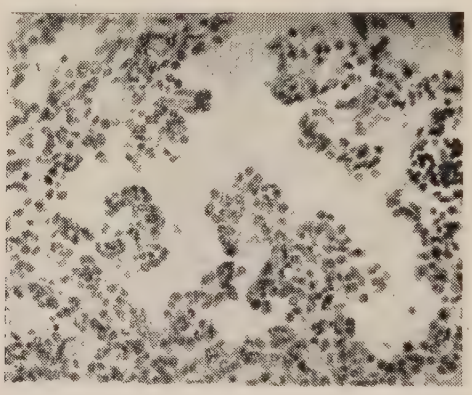

Fig. 18. Pulmonary tissue of immature fetus, with unmistakable lumina, but construction of the walls similar to that of non-aerated lungs. (Case K 425/45 B. Birth weight 670 gm. Hematoxylin and van Gieson. × abt 200.)

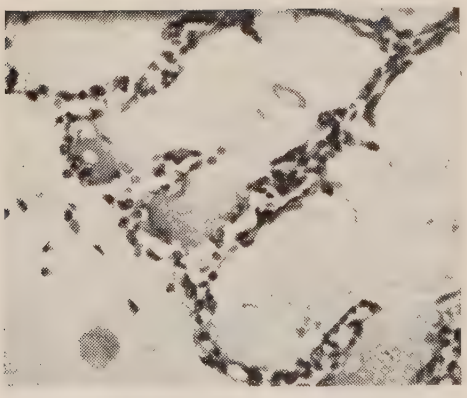

Fig. 19. Extended lumina in the areas below the pleura in the lungs of an immature fetus. It died in the course of the delivery. (Case N 352/II/45. Birth weight 1040 gm. Hematoxylin and eosin. × abt 200.)

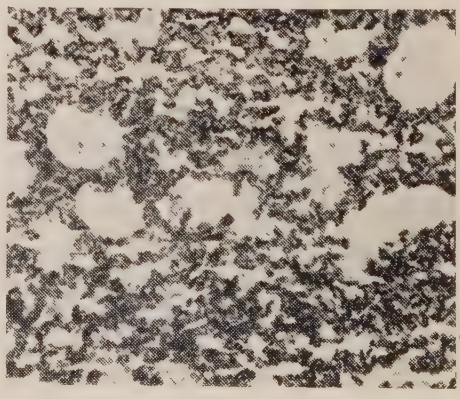

Fig. 20. Partly aerated lung of premature infant who died during delivery. Air-containing lumina have »tense walls». Medium amounts of aspirated substances in the lungs. (Case N 1521/II/45. Birth weight 2000 gm. Hematoxylin and eosin. × abt 100.)

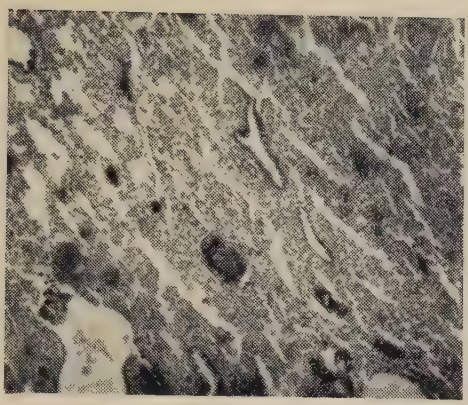

Fig. 21. Lungs of immature infant affected with secondary atelectasis. It survived for five days. (Case P 203/45. Birth weight 970 gm. Hematoxylin and eosin. × abt 50.)

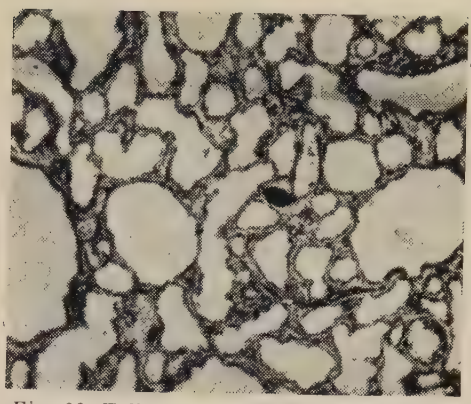

Fig. 22. Fully expanded lung of immature baby. It survived for one hour and a half. (Case K 720/45. Birth weight 920 gm. Masson's staining. × abt 50.)

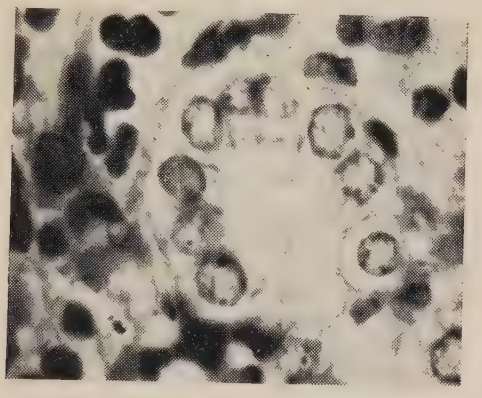

Fig. 23. Pneumonomeres of premature infant. The structure is regular, the cells have a somewhat similar form and their arrangement is regular. Capillaries are scarse. Lumina are small, but clearly visible. The baby survived for 13 minutes. (Case N 788/I/45. Birth weight 1360 gm. Hematoxylin and eosin. × abt 900.)

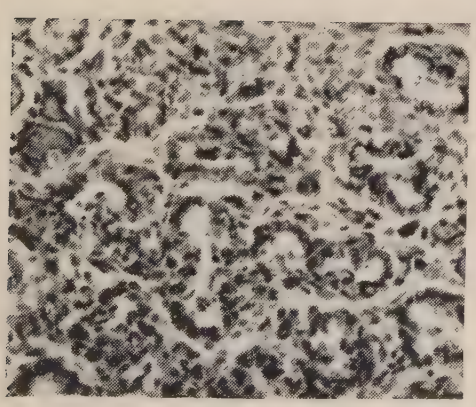

Fig. 24. Lung of premature who survived for half an hour. The fig. does not show air-containing lumina. — The structure is regular. Abundant amounts of loose tissue between the pneumonomeres. (Case K 2621/45. Birth weight 2080 gm. Hematoxylin and eosin. × abt 200.)

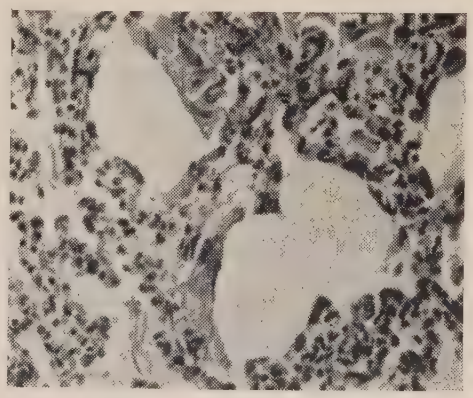

Fig. 25. Liquor amnii squamae are close to the walls in air-containing lumina. Lung of fullterm fetus who died during delivery. (Case K 643/46. Birth weight 3740 gm. Hematoxylin and eosin. × abt 200.)

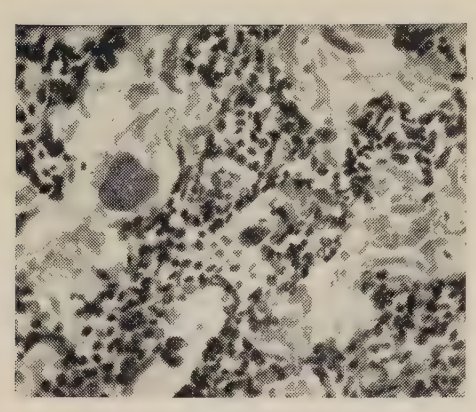

Fig. 26. Abundant aspiration of amniotic fluid in lungs of immature baby. It survived for two hours. (Case N 852/I/45. Birth weight 980 gm. Masson's staining. × abt 200.)

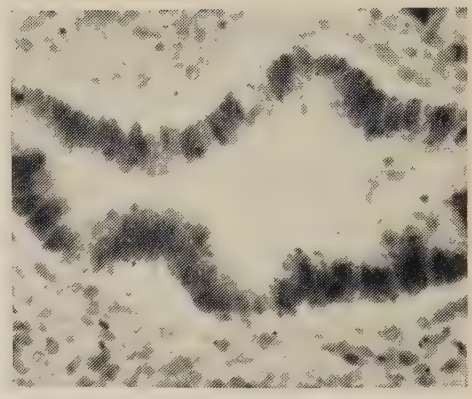

Fig. 27. Drops of fat in bronchial epithelium. Premature infant, survived for four hours. (Case 531/II/46. Birth weight 1560 gm. Sudan and hematoxylin. × abt 400.)

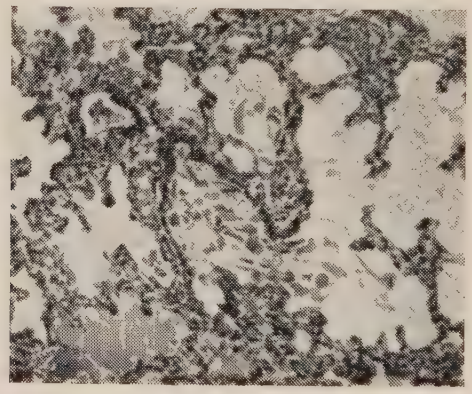

Fig. 28. Abundant quantity of amniotic fluid substances in »bronchioli». More to the periphery only precipitate in the lumina (same case as fig. 19. × abt 100.)

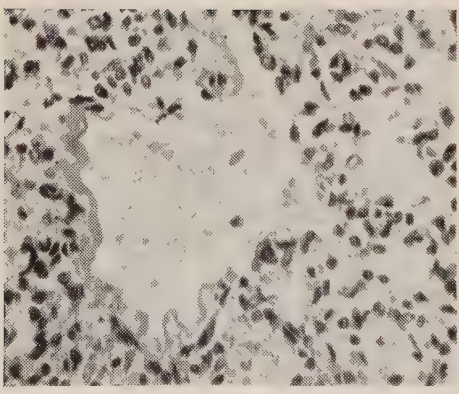

Fig. 29. Vernix membranes in lumina which contain precipitate. The membrane substances are not discernible in the figure. (Case N 494/II/45. Birth weight 2870 gm. Hematoxylin and eosin. × abt 200.)

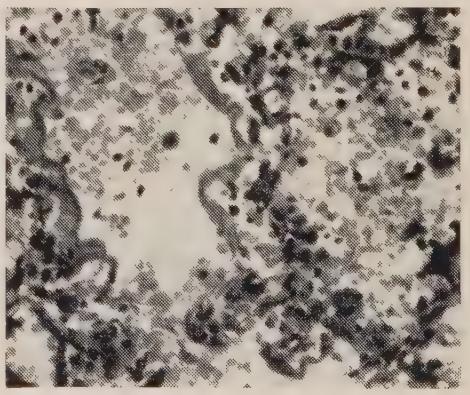

Fig. 30. Membranes in lungs whose lumina contain considerable amounts of blood. Full-term infant who lived for 13 days. (Case P 276/46. Hematoxylin and eosin. × abt 200.)

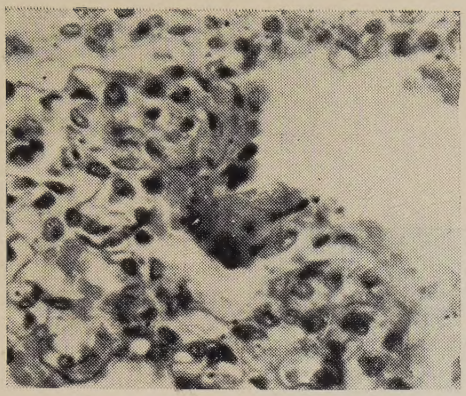

Fig. 31. Unmistakably air-containing lumina filled with a mass showing dark particles. This mass seems partly to be formed by cells coming off the walls. (Case N 2663/I/45 B. Birth weight 1470 gm. Hematoxylin and eosin. × abt 400.)

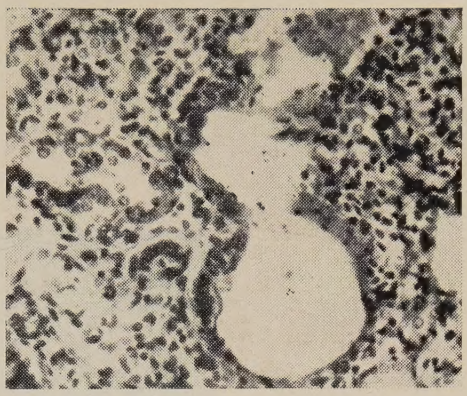

Fig. 32. Membranes in lung of immature baby. Membranes covering lumina with »tense walls». (Case L 94/46. Birth weight 920 gm. Hematoxylin and eosin. × abt 200.)

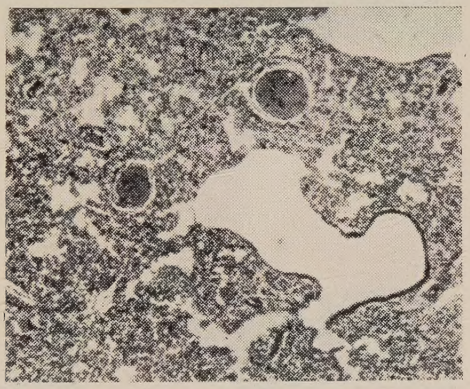

Fig. 33, Fig. 34, Fig. 35. Different degrees of expansion in the lungs of triplets N 519/II/46 A, B and C. The largest dilatation is unmistatably that of fig. 35 (Baby C). In fig. 33 (Baby A) and 34 (Baby B) the dilatation is about similar. The membranes of these cases are not visible in the figures. (Hematoxylin and eosin. × abt 50.)

Fig. 34.

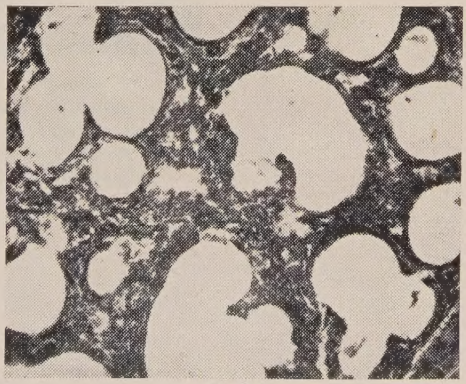

Fig. 35.

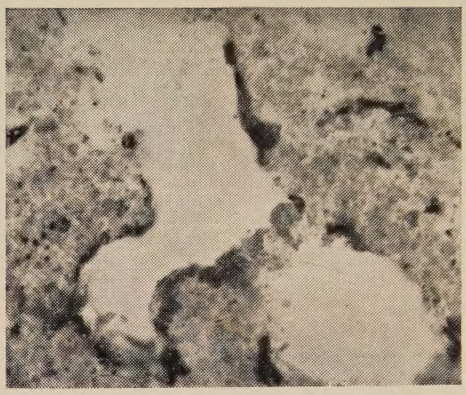

Fig. 36. Vernix membranes in the lungs of an infant who survived for four hours. (Case N 575/II/45. Birth weight 1070 gm. Sudan and hematoxylin. × abt 200.)

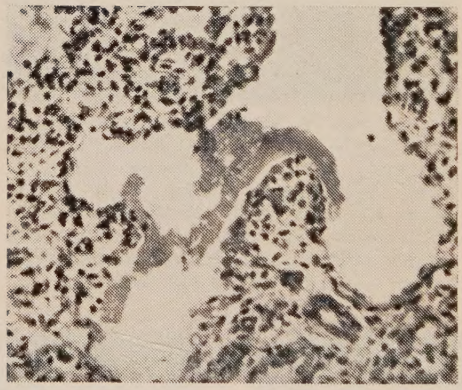

Fig. 37. Vernix membrane. Structure not discernible everywhere in the membrane, and it is of an almost homogeneous substance. (Case N 930/I/45 B. Birth weight 2220 gm. Hematoxylin and eosin. × abt 200.)